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Childhood Traumas: An Outline and Overview
By Lenore C. Terr

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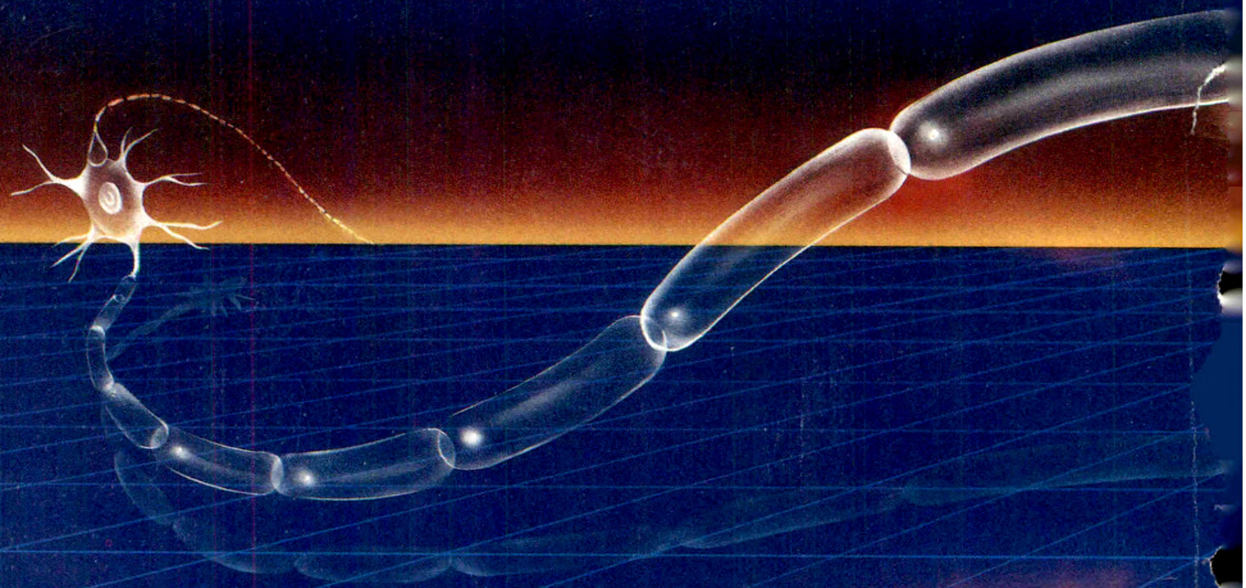

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THE AMERICAN JOURNAL OF PSYCHIATRY

Editorial

New Year's Greetings

William Butler Yeats, we suspect, spoke for authors everywhere when he wrote:

> Bald heads, forgetful of their sins,
> Old, learned, respectable bald heads
> Edit and annotate the lines
> That young men, tossing on their beds,
> Rhymed out in love's despair
> To flatter beauty's ignorant ear. (1)

—editorial "bald heads," indeed, who not only "edit and annotate" the lines offered for their critical judgment but, even worse, all too often reject them outright for publication in the periodicals entrusted to their editorship.

Limited by space in the *Journal* sufficient to include only one in five of the many hundreds of manuscripts submitted to him annually, the Editor must often appear to have a particularly "ignorant ear" to the majority of aspiring authors. His discomfiture at having to disappoint so many colleagues is, however, partially assuaged by the awareness that his editorial decisions are guided and informed by the expert knowledge of an extensive panel of selflessly devoted reviewers. It is, therefore, a pleasure to acknowledge our debt and gratitude to the following men and women for their never failing wisdom and advice during the period from November 1, 1989, to September 30, 1990.

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1990 has brought the *Journal* the proverbial mixture of "good news and bad news." The month of June was brightened by the birth of a daughter, Allison, to Ms. Melanie Shipley, our Managing Editor, and her husband. Ms. Shipley had fully intended to return to her editorial duties after a period of maternity leave, but, having discovered the joys of motherhood, she found that that responsibility had become a priority and submitted her resignation from her position on the *Journal* staff in August. Ms. Shipley will be sorely missed. In the relatively short time she was the *Journal*'s Managing Editor, she introduced major, innovative changes in its operation that will remain firmly in place. She goes with our deep gratitude and affection for her personal and professional contributions. In the face of Ms. Shipley's departure, we are fortunate indeed to have the continued services of Ms. Linda Loy, who, as Acting Managing Editor, has picked up the reins and with the unflagging help of her staff has kept our editorial operations moving forward smoothly and effectively. We must express as well our deep appreciation to the *Journal*'s Deputy Editor, Dr. Nancy C. Andreasen, and its Statistical Editors, Drs. John J. Bartko and Lee Gurel, who have not only shared the editorial burden with enthusiasm but brought unique talents to our editorial task. We must also record with sadness the departure from our Editorial Board of three greatly valued veteran Associate Editors, Drs. Jonathan F. Borus, Loren H. Roth, and Charles E. Wells, whose terms of office were completed at the end of the 1990 Annual Meeting. Our regret at their loss has been tempered by our good fortune in welcoming three outstanding new members to the Board in the persons of Drs. Paul S. Appelbaum, Gary J. Tucker, and George E. Vaillant.

At a time when matters fiscal and administrative are playing an ever increasing role in our professional lives, we continue to be grateful to our Medical Director, Dr. Melvin Sabshin, for his guidance and wisdom, and appreciate the support that he and the Board of Trustees have provided us in the performance of our editorial duties. For their help in numerous ways, we must express our gratitude, too, to Drs. Robert J. Campbell III, John Hamilton, William A. More, Harold A. Pincus, Carolyn B. Robinowitz, Jeanne Spurlock, John A. Talbott, and Jack W. White; to Mses. Laura Abedi, Teddye Clayton, Jacqueline Coleman, Carol Davis, Brenda Fasnacht, Nancy Frey, Debbie Goldberg, Melissa Hiett, Joan Lefkowitz, Karen Loper, and Beth Prester; and to Messrs. William E. Baxter, John Blamphin, George Campbell, Herbert M. Gant, Joel Klein, Ronald McMillen, and Raymond J. Purkis, Jr.

As 1990 ends and the countdown toward the millenium begins, we wish all of our colleagues a Happy New Year and a safe passage through the twelve months ahead.

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J.C.N.

Robert Hanna Felix, M.D.
1904–1990

Psychiatry recently lost one of its most outstanding leaders, but he left us with a marvelous legacy. That legacy has directly or indirectly influenced favorably the lives of thousands of professionals in the mental health and mental-health-related fields, the millions of patients they served, and the patients' relatives, friends, and neighbors. His contributions to all these and our country have been, and will continue to be, enormous.

Robert Hanna Felix, the eighty-ninth president (1960–1961) of the American Psychiatric Association, the architect and first director of the National Institute of Mental Health, and Dean Emeritus of the School of Medicine of St. Louis University, died at his home in Sun City, Ariz., on March 31, 1990, at the age of 85. He is mourned by his wife, Esther (Peg), their daughter, Mary Katherine (Kathy) Hoenigman, and two grandchildren (Robert and Rebecca). To these must be added his legion of friends and colleagues.

Dr. Felix (Bob) was ever mindful of the fact that psychiatrists, as medical specialists, must not only possess certain essential human qualities but also remember that they are, first of all, physicians. This view he urged upon his fellow specialists. "The good physician must have honor and integrity and a genuine respect and regard for his patient. . . . In addition, there is certain technical knowledge he must also

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possess without regard to his type or degree of specialization" (1, p. 4). "Just as the son is the child of his father, so is psychiatry the child of medicine" (1, p. 8).

Just so, he was the child of *his* father. The latter was a country doctor in Downs, Kan., who possessed special training in languages, history, and religion. His mother was a pioneer physician's daughter and a concert pianist. As a boy, Bob, who was known as "Little Doc," accompanied his father on house calls, experiencing from earliest childhood the important interplay of professional skills, respect, and concern for others. As his biographer, Dr. Francis Braceland, put it, he developed an "image of himself as a physician—he had it then, he has it now, and will always have it, no matter how far from the bedside he strays" (2, p. 10).

To these strong basic ingredients were added the influences of the Downs public schools and the University of Colorado's premedical and medical curricula (he received his M.D. in 1930), internship, and psychiatric residency program. He was a Commonwealth Fund Fellow during his residency years (1931–1933) at Colorado Psychopathic Hospital, where Dr. Franklin Ebaugh, his chief, not only exposed him to intense clinical teaching but also stimulated a great interest in community psychiatry and public service. These interests were further nurtured at The Johns Hopkins School of Hygiene and Public Health (he received the degree of M.P.H. in 1942), where he came to appreciate the importance of clarifying the epidemiology of the many different forms of mental disorder. There, according to a fellow student, he "began to think of communities (as well as individuals) as patients. He also presented, as a class exercise in Public Health Administration, a 'national program for mental health' that foreshadowed the future National Mental Health Act" (Harold J. Magnuson, personal communication, 1990). A final formal learning experience, in the late 1940s, consisted of a training psychoanalysis with Dr. Frieda Fromm-Reichmann.

It was during his residency that he met and married (in 1933) Esther Wagner, a nurse on the staff of Children's Hospital and the love of his life. In 1945 they became the more-than-proud and devoted parents of Mary Katherine, a much-wanted child. She, in turn, became the mother of their adored grandchildren. Bob's family played a central role throughout his life.

Upon the completion of his residency, Dr. Felix was commissioned as an assistant surgeon in the commissioned corps of the U.S. Public Health Service. His first duty assignment was at the medical center for federal prisoners at Springfield, Mo., and this was followed by 5 years at the U.S. Public Health Service hospital at Lexington, Ky. The latter was the first federal hospital devoted to the treatment of drug addicts and to the pursuit of rigorous research into the causes of addiction and the treatment of drug-dependent persons. During those years, he benefited from exposure to unusual types of clinical material seen in quantity by very few psychiatrists. And his participation in rigorously controlled research, in association with professional colleagues from a variety of professional disciplines, was an experience shared by only a minuscule number of young psychiatrists at that time. Dr. Felix's research interests and skills were further honed while he was assigned to the U.S. Coast Guard Academy at New London, Conn. (1942–1944), where he was responsible for implementing "an integrated medico-psychological program" (3). That program involved a major, interdisciplinary research undertaking on the selection of officer candidates. In 1944 he was transferred from the academy to Washington, D.C., where, standing on the shoulders of other big men, he stood tall in making his own major contributions to American psychiatry and mental health.

Among those on whose shoulders he stood was Dr. Lawrence Kolb, his mentor in the Public Health Service, the man who chose him to go to The Johns Hopkins University for training in public health and who was his immediate predecessor as chief of the Mental Hygiene Division of the Public Health Service. In the 1930s Dr. Kolb had envisioned the creation of a national neuropsychiatric institution within the Public Health Service to lead a concerted attack on the mysteries of mental illness, which then accounted for over half of the hospitalized patients in the United States. However, World War II intervened.

So it was that, in anticipation of Dr. Kolb's retirement, Bob was called to Washington by Surgeon General Thomas Parran and shortly thereafter given responsibility for direction of the Mental Hygiene Division. Dr. Parran was another of the giants on whose shoulders Bob stood. Of Dr. Parran, a pioneer in the fields of venereal disease and tuberculosis control, Dr. Felix said, "His insight into the mental health needs of this country was phenomenal. . . . The program would never have gotten off the ground without his support with the Bureau of the Budget, the Department, and with Congress" (2, p. 11). But what was the program that became Bob's enormously valuable contribution to his country and his profession?

He presented a "blueprint for mental public health" which called for

> the erection of a structure with several wings, all of which are functionally interrelated. Therefore, the foundations for all the elements must be laid and construction begun at the same time. It will not be possible to complete each part at the same time; but each part must be at some state of completion at all times. The efforts toward the specific objectives must be parallel. . . .
>
> The several parts of the plan are:
>
> 1. Training of personnel.
> 2. Psychiatric services for case-finding, and for diagnosis and treatment of persons who do not require institutional care.
> 3. Improved services in mental hospitals.
> 4. Education of the public.
> 5. An augmented and coordinated program of research (4).

Under Bob's guidance, and with the help and support of countless individuals and organizations, the National Mental Health Act was signed into law on July 3, 1946. It provided for 1) support of research through the development of a system of grants-in-aid to institutions and individuals, the construction of a National Institute of Mental Health in the Washington area, and the appointment of research Fellows in various scientific fields that bear upon mental health problems; 2) support of training through a system of grants-in-aid to public and other nonprofit institutions; and 3) support of community mental health services through a system of matching grants-in-aid to the states (5).

The act also provided for the appointment of a National Advisory Mental Health Council to guide the program. Grants-in-aid for research and training projects could be made only with the approval of that council. Thus was provision made for broad policy advice and peer review.

As a comment on the usefulness of the program, I can do no better than to quote, once again, Bob's 1961 biographer, Francis Braceland: "The amount of good this Institute has done for the cause of mental health is incalculable. To even hint at the scope of its research and teaching efforts would be far beyond our purview here. Without its farsighted planning and help, the whole psychiatric picture in this nation would be one bordering on chaos" (2, p. 12).

Upon his retirement in 1964 from the Public Health Service, where in 1957 he had attained the rank of Assistant Surgeon General, Bob accepted an invitation to become Dean of the School of Medicine at St. Louis University. There he endeared himself to all. Of him, the current Dean, Dr. William Stoneman III, said, "Dr. Felix served as Dean at St. Louis University School of Medicine from 1964 to 1974. During this vigorous decade, the full-time faculty increased 300%; the total enrollment, 36%. Student performance on National Board Examinations rose dramatically and consistently. . . . He opened doors and windows never before tried, he wrought profound change, and left an institution which would never be quite the same as it was before his leadership left its mark" (personal communication, 1990). The Rev. Paul C. Reinert, S.J., Chancellor of the University, upon learning of Bob's death, said, "His ability to rally the enthusiasm and support of every person in the Medical Center—administrators, faculty, alumni, and students—was remarkable. His openness and spirit of optimism gave us all a new perspective on how promising the future of the Medical Center might be" (personal communication, 1990).

In 1974 Dr. Felix not only became Dean Emeritus but also took on the task of serving as program director for the Bi-State Regional Medical Program in St. Louis, a program dedicated to bringing all available resources and interests to bear on improving the health of the community.

Bob and Peg moved from St. Louis to Sun City, Ariz., for their well-deserved retirement in December 1976. But even then, he didn't *really* retire. He continued actively serving as research director of the Scottish Rite Schizophrenia Research Program of Lexington, Mass. (1975–1985), played an active role in his church (as he had all his life), and served on the board of directors of Interfaith Services, an organization of over 100 churches and social agencies. He was the prime mover in developing its case management service, which currently responds to more than 300 calls per month from persons needing some form of community help.

During his lifetime, Dr. Felix was the recipient of six honorary doctoral degrees from as many universities, as well as the APA Distinguished Service Award in 1974 and other honors and awards too numerous to detail here. He was also an active member of many professional and fraternal organizations, editorial boards, councils, and committees.

Let me close this tribute to a great man, who was my close friend and colleague of 50 years, by quoting his comment to someone with whom he shared great affection and respect, Gloria O'Connor. She was his principal secretary during his years as Dean. As he bid her a fond farewell upon his departure from that office, he said, "Remember, when you hear that something has happened to me, that I have had a full life, that I have tasted its sweetness, that I have gotten back far more than I had any right to expect, so be happy" (personal communication, 1990).

We really are *not happy* about his leaving, but we are *awfully glad* he came! His legacy will live on.

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Childhood Traumas: An Outline and Overview

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Childhood psychic trauma appears to be a crucial etiological factor in the development of a number of serious disorders both in childhood and in adulthood. Like childhood rheumatic fever, psychic trauma sets a number of different problems into motion, any of which may lead to a definable mental condition. The author suggests four characteristics related to childhood trauma that appear to last for long periods of life, no matter what diagnosis the patient eventually receives. These are visualized or otherwise repeatedly perceived memories of the traumatic event, repetitive behaviors, trauma-specific fears, and changed attitudes about people, life, and the future. She divides childhood trauma into two basic types and defines the findings that can be used to characterize each of these types. Type I trauma includes full, detailed memories, "omens," and misperceptions. Type II trauma includes denial and numbing, self-hypnosis and dissociation, and rage. Crossover conditions often occur after sudden, shocking deaths or accidents that leave children handicapped. In these instances, characteristics of both type I and type II childhood traumas exist side by side. There may be considerable sadness. Each finding of childhood trauma discussed by the author is illustrated with one or two case examples.

(Am J Psychiatry 1991; 148:10–20)

Mental conditions brought on by horrible external events in childhood present a wide range of findings. If one looks only at the clinical manifestations of trauma in a given day in the life of the traumatized child, one could diagnose conduct disorder, borderline personality, major affective disorder, attention deficit hyperactivity, phobic disorder, dissociative disorder, obsessive-compulsive disorder, panic disorder, adjustment disorder, and even such conditions, as yet unofficial in the nomenclature, as precursors of multiple personality or acute dissociative disorder, and not be wrong. If one projects this multiplicity of technically correct diagnoses onto a traumatized child's adulthood, one finds even more diagnostic leeway.

We must organize our thinking about childhood trauma, however, or we run the risk of never seeing the condition at all. Like the young photographer in Cortázar's short story and Antonioni's film, "Blow Up," we may enlarge the diagnostic fine points of trauma into such prominence that we altogether lose the central point—that external forces created the internal changes in the first place. We must not let ourselves forget childhood trauma just because the problem is so vast.

Studies of adults in mental hospitals (1), adults suffering from multiple personalities (2), adults who are borderline (3), and adolescents who go on to commit murder (4) show that these adults and adolescents very often were abused or shocked in their own childhoods. Studies of adult rape victims demonstrate that they often were raped or incestuously abused as children and that they are quite prone to being raped again—and again—in their adult lives (5). Those who harm children have often been harmed themselves as chil-

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dren (6). And some of those who indulge in self-mutilation or who make repeated suicide attempts give vivid past histories of long-standing childhood horrors (7).

One could say that childhood trauma is so ubiquitous to the psychiatric disorders of adolescence and adulthood that we should forget it, that it cancels itself out. We know, however, that not every child is directly shocked or personally subjected to terror from the outside. Most children come from relatively kind, nonabusive families. Most youngsters are never enrolled in a pedophilic day-care center or happen upon a satanic cult. The chances of experiencing a frightening flood, hurricane, or earthquake are not that great. The chances of witnessing a murder or of being kidnapped are not overwhelmingly high. Numbers of children should be able to get through their childhoods without any direct exposure to a traumatic event or series of terrible events. And they apparently do so (8, 9).

Even if we were to broaden the diagnosis of childhood trauma, as I will propose in this paper, to allow in any child mentally harmed enough by a single external event or a long-standing series of such events to qualify for a trauma-related diagnosis, we could not possibly cover everything that we see in adults as a result of these early traumas—the borderline patients, the patients with multiple personality disorder, and the chronic victims or victimizers, for instance. We will still need our adult diagnostic schemes and our adult treatment plans. But perhaps, if we looked in a more organized fashion at childhood psychic trauma and at what it does, we would recognize it as the important etiologic determinant that it actually is. We could begin to see how childhood trauma works. And we could study it better.

Like childhood rheumatic fever, which causes a number of conditions in adulthood ranging from mitral stenosis to subacute bacterial endocarditis to massive heart failure, childhood psychic trauma leads to a number of mental changes that eventually account for some adult character problems, certain kinds of psychotic thinking, considerable violence, much dissociation, extremes of passivity, self-mutilative episodes, and a variety of anxiety disturbances. Even though heart failure and subacute bacterial endocarditis in adulthood look very different from one another and demand specific treatments, their original cause—the childhood rheumatic fever—gives an organizing pattern to the physician's entire approach. Every good internist knows how to obtain and assess a history of rheumatic fever, even though it was the pediatrician who originally diagnosed and treated the sick child.

In this paper, I will define childhood trauma and point to four features that characterize almost all of the conditions resulting from extreme fright in childhood. These four features are seen in children suffering the results of events that were single, sudden, and unexpected, the classical Freudian traumas (10, 11), and in children responding to long-standing and anticipated blows, those resulting in the various child abuse syndromes (12, 13) or survivor syndromes (14–16). These four features appear to last for years in the course of the condition. They are often seen in adults who were traumatized as children, even though the adults now carry other diagnoses. Only one or two of these four features may be evident in an individual traumatized as a child; but from the history it is often evident that the other features played an important part in the person's life.

I will divide all of the trauma-stress conditions of childhood into two rough categories and call them type I and type II childhood traumas. I will propose that children suffering from type I traumas, the results of one sudden blow, differ in certain ways from children suffering from type II traumas, the results of long-standing or repeated ordeals. I will conclude with a note on the crossover conditions, childhood traumas that appear to settle between the two major types that I propose.

This paper is largely theoretical, although each point will be illustrated with a clinical example. It is based, in part, upon three studies: the Chowchilla kidnapping study (8, 17, 18), a retrospective study of 20 preschoolers suffering from a wide range of traumas that were documented by third parties (19), and a study of normal latency-aged children's and adolescents' responses to the Challenger space shuttle explosion (9). The paper is primarily based, however, upon my clinical notes taken from more than 150 individual children who came for evaluation or treatment after a variety of externally generated horrors. The paper is an attempt to organize and to provide a scheme of thinking about childhood psychic trauma. It is not meant in any way as a last-minute addition to the *DSM-IV* process or as a proposal for a new and revisionary *DSM-V*. Instead, it is an outline and overview of a group of phenomena that may go their various ways into the adult diagnostic groups but that should still hold together in our thinking because of their association with the earliest traumas.

I will define childhood trauma as the mental result of one sudden, external blow or a series of blows, rendering the young person temporarily helpless and breaking past ordinary coping and defensive operations. As the reader will note, I have broadened the concept of trauma to include not only those conditions marked by intense surprise but also those marked by prolonged and sickening anticipation. All childhood traumas, according to my definition, originate from the outside. None is generated solely within the child's own mind. Childhood trauma may be accompanied by as yet unknown biological changes that are stimulated by the external events. The trauma begins with events outside the child. Once the events take place, a number of internal changes occur in the child. These changes last. As in the case of rheumatic fever, the changes stay active for years—often to the detriment of the young victim.

FOUR CHARACTERISTICS COMMON TO MOST CASES OF CHILDHOOD TRAUMA

There are several well-known characteristics that distinguish the traumas of childhood. Thought suppression, sleep problems, exaggerated startle responses, developmental regressions, fears of the mundane, deliberate avoidances, panic, irritability, and hypervigilance are prominent among these.

I consider four characteristics, however, particularly important in traumatized children no matter when in the course of the illness one observes the child and no matter what age the child is at the time. They are: 1) strongly visualized or otherwise repeatedly perceived memories, 2) repetitive behaviors, 3) trauma-specific fears, and 4) changed attitudes about people, aspects of life, and the future.

One note on traumatic dreams, the classic Freudian sign of trauma that I have not included in my list of four: the repetitive dream is a hallmark of trauma, but it is not always seen in childhood trauma, especially in children under age 5. Dreaming appears to be something that develops into what we recognize as dreaming by about age 3 or 4 (20). Before that, infants physically demonstrate that they are dreaming by making mouthing movements or little sounds in their sleep. Toddlers may scream from sleep without awakening, but this kind of dreaming is often too primitive and inexpressive to establish that traumatic dreams are actually taking place (21). In a study of 20 children with documented traumas that occurred before the age of 5, only four of them verbalized the contents of their dreams (19). The repeated dream apparently is very difficult to find in most traumas before the age of 5. Furthermore, these dreams often take deeply disguised forms as time progresses after the traumatic event. In those children old enough to dream and to remember their dreams, traumatic dreaming may occur at intervals several years apart or in such deeply disguised forms that the process becomes extremely difficult to distinguish from other forms of dreaming.

Visualized or Otherwise Repeatedly Perceived Memories

The ability to re-see or, occasionally but less frequently, to re-feel a terrible event or a series of events is an important common characteristic of almost all externally generated disorders of childhood (22). Re-seeing is so important that it sometimes occurs even when the original experience was not at all visual (22). Tactile, positional, or smell memories may also follow from long-standing terrors or single shocks. But the tendency to revisualize appears to be the strongest of all of these re-perceptions in childhood trauma. Visualizations are most strongly stimulated by reminders of the traumatic event, but they occasionally come up entirely unbidden.

The vivid and unwelcome nature of returning traumatic visualizations marks them as special to these externally generated conditions. Children tend to see their traumas and old ordeals at leisure—during times when they are bored with classes, at night before falling asleep, and when they are at rest listening to the radio or watching television. As opposed to those traumatized as adults, traumatized children rarely find themselves abruptly interrupted by sudden, dysphoric visualizations.

Even those who were infants or toddlers at the time of their ordeals and thus were unable to lay down, store, or retrieve full verbal memories of their traumas tend to play out, to draw, or to re-see highly visualized elements from their old experiences (19). In cases in which the facts of a sexual abuse are not known, for instance, children may indicate their internalized visions of the abuse by sketching what they see in their mind or acting it out almost like a movie picture. Such children may use their visual and positional senses, senses that may outlast the verbal memory itself, to draw pictures of themselves "at the most scary moments of [their] life." Of course, other posttraumatic features should be present, too, if the child actually was a trauma victim.

Three and a half years after experiencing a series of traumatic events, a 5-year-old child was discovered (through pornographic photographs confiscated by U.S. Customs agents) to have been sexually misused in a day-care home between the ages of 15 and 18 months. The girl's parents did not dare speak to her about what they had learned from the investigators. They, in retrospect, realized that she had been sketching hundreds of nude adults beginning from the time when she had first begun to draw.

While playing in my office, this child told me that a baby she had just drawn was "all naked" and "a bad girl." Unknowingly, she had just depicted herself. Despite the fact that the little girl's only verbal memory of the events was "I think there was grave danger at a lady—MaryBeth's—house," her volumes of drawings represented strongly visualized elements that she had retained and had needed to recreate from these very early, nonverbal experiences.

A 40-year-old mental health professional began working at a facility for male juvenile delinquents. On his long rides home he began seeing himself as a toddler—attacked in a shack by a group of older children. The man drove to the town where he had lived until he was 4 years old, and he found the shack that he had "pictured." The shack stood catercornered to his old house.

Repetitive Behaviors

Play and behavioral reenactments are frequent manifestations of both the single blow and the long-standing terrors of childhood. Psychophysiologic repetitions are less frequently observed in ordinary practice, but they gain particular importance in certain cultures (23). Posttraumatic play, defined by the players as "fun," is a grim, long-lasting, and particularly contagious form of childhood repetitive behavior (24). Although reenactments lack the element of "fun," they also repeat aspects of the terrible events. Reenactments can occur as single behaviors, repeated behaviors, or bodily responses. Repetitive behaviors may even be seen in children who were exposed to traumatic events before the age of 12 months (19). In other words, children who have no verbal memory whatsoever of their traumas may be seen to feel physical sensations or play or act in a manner that evokes what they originally experienced at the time of the event. The 5-year-old girl described in the previous case vignette, for instance, experienced "funny feelings" in her "tummy" every time she saw a finger pointed at her. The pornographic pictures confiscated by the customs authorities showed an erect penis jabbing the very spot on the 15–18-month-old child's belly that she had indicated when, at age 5, she spoke of the "funny feelings."

The childhood survivors of single shocks and of long-standing terrors are usually entirely unaware that their behaviors and physical responses repeat something of the original set of thoughts or emergency responses. Thus, the presence or absence of behavioral reenactments may at times be better determined from interviews with third parties.

Behavioral reenactments may recur so frequently as to become distinct personality traits. These may eventually gather into the personality disorders of adulthood, or they may recur so physiologically as to represent what seems to be physical disease. Long after most repeated nightmares have disappeared into deeply disguised form, reenactments continue to characterize the behaviors of traumatically stressed children. Recent psychiatric investigation into the lives and works of important artists—Edgar Allen Poe, Edith Wharton, René Magritte, Alfred Hitchcock, and Ingmar Bergman (25), Stephen King (26), and Virginia Woolf (27)—show that these artists reenacted childhood traumas behaviorally throughout their lifetimes and also played out their traumas in artistic works spanning their entire careers. If one could live a thousand years, one might completely work through a childhood trauma by playing out the terrifying scenario until it no longer terrified. The lifetime allotted to the ordinary person, however, does not appear to be enough.

A 6-year-old girl walked into a circus tent and was suddenly attacked by a runaway lion. The animal tore open her scalp and bit into her face. The girl had to undergo several surgical procedures to repair what happened within a few seconds' time. She was left with an uneven hairline and a large bald spot. After the extraordinary experience, the little girl preferred "Beauty Parlor" to all other games of pretend. She combed her younger sister's hair repeatedly, often bringing the younger child to tears over the roughness of the combing. The little girl's dolls developed bald spots and uneven hairlines without anyone ever observing exactly how these anomalies came into being. The child, previously outgoing and friendly, stuck close to home and rarely ventured out into her neighborhood. At age 6, her main hopes for the future were to grow up and become a runway model or a "beauty parlor lady."

Trauma-Specific Fears

Some of the specific fears related to the shocks and long-standing extreme external stresses of childhood can be avoided by moving out of town or by changing houses or neighborhoods. Fears can be conditioned away by repeatedly facing the feared object. Most extremely stressed or psychically traumatized children continue to harbor one or two trauma-related fears, however, well into adulthood. Fears of specific things that are related to experiences precipitated by traumatic events are fairly easy to spot, once one knows what the trauma might have been. This type of literal, specific fear is pathognomonic of the childhood traumas. Whereas neurotically or developmentally phobic children may fear *all* dogs, the dog-bitten youngster will fear the German shepherds, the Dobermans, or whatever species actually created the traumatic state. Whereas neurotically anxious children fear growing up or getting married, traumatized youngsters fear (and re-create) oral sex, anal intercourse, or whatever particular sexual abuse they originally experienced.

Traumatized children tend also to fear mundane items—the dark, strangers, looming objects, being alone, being outside, food, animals, and vehicles, for instance. In fact, fears of the dark and of being alone are strongly connected with sudden shocks in the early years (9). But these mundane fears may also be connected with a number of other emotional disorders and developmental stages of childhood. The panic and extreme avoidances observed following terrifying events, in connection with this mundane group of fears, *do* make them important to childhood trauma. But the specific, literal kinds of fear noted in the preceding paragraph almost "label" the traumatic condition. When one sees this literal kind of fear lasting throughout the years despite the natural tendencies toward spontaneous desensitization, childhood trauma is the most likely cause.

A girl was sexually misused by her father from age 5 to age 15, at which time she ran away from home, never to return. As a married adult of 38, she feared sex with her husband unless she initiated the act herself. She responded to the female-on-top or side-to-side positions, positions that had not originally been taken by her father. Any sexual positioning that was evocative of the incestuous set of sexual postures stimulated fear, pain, and revulsion.

Changed Attitudes About People, Life, and the Future

The sense of a severely limited future, along with changed attitudes about people and life, appears to be important in the trauma and extreme stress disorders originating in childhood. The limitation of future perspective is particularly striking in traumatized children because ordinary youngsters exhibit almost limitless ideas about the future. Truisms, such as "I live one day at a time" or "I can't guess what will happen in my lifetime," come from the rethinkings that occur in the years after traumatic events. Ideas such as "You can't trust the police" or "You can't count on anything or anyone to protect you" also follow from single and long-standing, repeated traumas. Sexually traumatized girls may shrink away from men or accost them with overfriendly advances. Part of this behavior is reenactment, but part reflects attitudinal changes. Limitations in scope and future perspective in childhood trauma victims seem to reflect the ongoing belief that more traumas are bound to follow. Traumatized children recognize profound vulnerability in all human beings, especially themselves. This shattering of what Lifton and Olson call "the shield of invincibility" (28) and what Erikson terms "basic trust" and "autonomy" (29) appears to characterize almost all event-engendered disorders of childhood. The feeling of futurelessness of the traumatized child is quite different from that of the depressed youngster. For the traumatized, the future is a landscape filled with crags, pits, and monsters. For the depressed, the future is a bleak, featureless landscape stretched out to infinity.

A 17-year-old boy, searching for a freeway shoulder on which to stop his disabled car, was hit from the rear by a speeder. The boy's automobile exploded. He flew out completely unscathed but watched helplessly as his best friend burned to death in the passenger seat.

For months after the event the boy could not work and spent most of his days moping. He was plagued with bad dreams and fears of further disaster. He began psychotherapy; and when I said to him at the end of an early session, "See you next week," he asked, "How do you know it will be next week? Who knows? I may die on my way out of your office. I may be killed out there on the sidewalk. I don't count on seeing you next week. I live day to day—day to day."

A 15-year-old girl came for psychiatric treatment because, since she was attacked at age 8, she had failed to volunteer or speak up in class. Since her acceptance in an academic high school, she could achieve no more than Bs because she was too quiet.

The girl had experienced significant changes in her attitudes about life and people while she was lying in a hospital room for 3 months, following repairs to her vagina, anus, and peritoneum. A man had grabbed her from a Chinatown sidewalk on her way home from school. He had taken her into an abandoned garage and attacked her vagina with a pair of chopsticks. The girl had decided after her ordeal that she was "chosen" by the deranged man because she had "showed too much." Never again, she had vowed to herself, would she ever "show." People could not be trusted, she believed. Life must be endured, not savored.

FEATURES CHARACTERISTIC OF THE SINGLE-BLOW TRAUMAS, TYPE I DISORDERS

The type I traumatic conditions of childhood follow from unanticipated single events. These are classical childhood traumas by Anna Freud's definition (30). These are also the most typical posttraumatic stress disorders that one finds in childhood, usually meeting the criteria of repetition, avoidance, and hyperalertness that represent the major divisions in our diagnostic manual, *DSM-III-R*. Those children who suffer the results of single blows appear to exhibit certain symptoms and signs that differentiate their conditions from those resulting from the more complicated events. The findings special to single, shocking, intense terrors are 1) full, detailed, etched-in memories, 2) "omens" (retrospective reworkings, cognitive reappraisals, reasons, and turning points), and 3) misperceptions and mistimings. Type I traumas do not appear to breed the massive denials, psychic numbings, self-anesthesias, or personality problems that characterize the type II disorders of childhood.

Full, Detailed Memories

With the exception of youngsters below the approximate age of 28 to 36 months, almost every previously untraumatized child who is fully conscious at the time that he or she experiences or witnesses one terrible event demonstrates the ability to retrieve detailed and full memories afterward (19). Verbal recollections of single shocks in an otherwise trauma-free childhood are delivered in an amazingly clear and detailed fashion. Children sometimes sound like robots as they strive to tell every detail as efficiently as possible. As a matter of fact, children are sometimes able to remember more from a single event than are the adults who observed the same event (24). A few details from a traumatic event of childhood may be factually wrong because the child initially misperceived or mistimed the sequence of what happened. But children with type I disorders seem to remember the event and to give impressively clear, detailed accounts of their experiences.

This remarkable retrieval of full, precise, verbal memories of almost all single-blow traumas makes one conclude that these memories stay alive in a very special way, no matter how much conscious suppression the traumatized child is attempting. Memories of prolonged or variably repeated childhood abuses, on the other hand, appear to be retained in spots, rather than as clear, complete wholes (19). Amnesias, as a matter of fact, are often reported in children who seem to be heading for the multiple personality disorders of adulthood (31). Children who have been repeatedly physically or sexually abused may waver in their accusations of abusers and waver in the completeness and the detail of their memories. But children who have been traumatized a single time do not often forget. As Malle says at the conclusion of his autobiographical film, *Au Revoir Les Enfants* (1987), a tale of a single, terrible event from his boyhood in occupied France, "Over forty years have passed, but I will remember every second of that January morning until the day I die."

The first time that he visited the psychiatrist, a 5-year-old boy minutely described his stepfather's murder of his baby brother. The incident had occurred 2 weeks earlier. The boy knew just where under the television table in a motel room he had been hiding. He reported exactly where he had been sitting and lying before taking cover. He described the types of blows that fell upon his younger sibling and meticulously repeated the attacker's phrases and threats. He said that he had been trying to forget all of this but could not. The boy's teacher had been reprimanding him for repeatedly hiding under the desks and tables at school, but neither teacher nor student recognized the significance of this "bad behavior."

Omens

During and after single-blow shocks, children tend frequently to ask themselves "Why?" and "Why me?" In this way they attempt to gain retrospective mastery over the randomness, the lack of control, and the "less-than-humaneness" of the trauma that they endured. When children traumatized by a single event belatedly develop a reason why everything happened, a purpose to the entire affair, or a way that the disaster could have been averted, considerable mental energy goes into these reworkings of the past. I have termed these belated reshiftings, reasons, and warnings "omens" (17), while Pynoos et al. call them "cognitive reappraisals" (11). I believe that we are describing the same phenomenon. This kind of rethinking and reworking occurs much more often after one sudden external shock than it does after a prolonged series of terrible experiences. Children who have found omens or reasons to explain why they suffer often feel intensely guilty. Although victims of type II childhood trauma also experience profound guilt, the sense of guilt does not often consciously align itself to the "Why me?" question. The repetitions and long-standing nature of the type II stressors make the inquiry "How could I have avoided it?" far less pressing than the question "How will I avoid it the next time?"

The omen or cognitive reappraisal is a belated way in which the singly traumatized child tries to deal retroactively with what had been entirely unexpected—a sudden, surprising psychological blow. Because repeated horrors encourage a sense of anticipation and expectation, different means of coping come to be employed. These means of coping eventually create the defining characteristics of the type II disorders, characteristics that are unmatched in the type I disorders.

An 8-year-old boy's mother bought him a fancy skateboard, admonishing him to ride only on the sidewalk. The first Saturday morning the boy rode his skateboard on the sidewalk, he was run over by a car backing out of a neighbor's driveway. The boy commented a year later, "I can't help thinking many, many times about what Mom said about riding skateboards on sidewalks."

A 16-year-old girl received a slice of pizza from her best friend as a birthday present. Biting into the pizza, she was poisoned by a corrosive toxin. The girl suffered from internal injuries for more than 6 weeks. Even though the real source of the poison was found by health officials at the pizza parlor, the injured girl thought again and again about the nature of her relationship with the friend who had purchased the pizza. In minutest detail she tried to figure out at what point her friend had decided to kill her.

Misperceptions

Misidentifications, visual hallucinations, and peculiar time distortions often occur to children who have experienced single, intense, unexpected shocks (22, 32). In contrast to this, the long-standing, extreme external stresses that affect children are often engineered by perpetrators known to them—caretakers, teachers, or family members, for instance. Because of a child's familiarity with such perpetrators, the chances of early misperceptions become slim. Two important exceptions to this general rule are when a type II victim thinks that he or she "sees" a once-familiar abuser years after losing track of the person and when a known, long-standing perpetrator was never perceived correctly by the child because of a disguise that he or she was wearing (as in satanism and cults).

Many of the type I childhood traumas include visual misperceptions and hallucinations. These perceptual distortions may seem to indicate organic mental conditions or psychoses, but a few bizarre sightings do not "make" a brain disorder or a schizophrenic episode. Visual hallucinations and illusions are observed in children shortly after traumatic events and, at times, long after sudden, unanticipated shocks. Massive releases of neurotransmitters in the brain at the time of the terror may account for these problems with perception. But the types of substances and mechanisms are, as yet, unknown.

A 7-year-old girl rode in a station wagon alongside her sister and two cousins on a family outing to the mountains. A loose boulder from an adjacent hillside smashed into the roof of the girl's car, killing one cousin and the girl's older sister, while sparing the girl and her other young cousin. For the ensuing year, the surviving girl "saw" her sister at her bedside almost every night. The dead sister visited the living child dressed in pink, green, and orange outfits. She appeared fully fleshed, as she was in life. The vision said nothing. The young survivor felt upset by a sense of menace emanating from her sister's "ghost," yet, at the same time, she felt oddly comforted by the sight.

FEATURES CHARACTERISTIC OF VARIABLE, MULTIPLE, OR LONG-STANDING TRAUMAS, TYPE II DISORDERS

Type II disorders follow from long-standing or repeated exposure to extreme external events. The first such event, of course, creates surprise. But the subsequent unfolding of horrors creates a sense of anticipation. Massive attempts to protect the psyche and to preserve the self are put into gear. The defenses and coping operations used in the type II disorders of childhood—massive denial, repression, dissociation, self-anesthesia, self-hypnosis, identification with the aggressor, and aggression turned against the self—often lead to profound character changes in the youngster. Even though a repeatedly abused youngster may not settle into a recognizable form of adult character disorder until the late teens or early twenties, extreme personality problems may emerge even before the age of 5.

The emotions stirred up by type II traumas are 1) an absence of feeling, 2) a sense of rage, or 3) unremitting sadness. These emotions exist side by side with the fear that is ubiquitous to the childhood traumas. Type II disorders, under the scrutiny of able mental health professionals, may come to be diagnosed in childhood as conduct disorders, attention deficit disorders, depression, or dissociative disorders. Recognition of the expanded group of traumas that I am suggesting here may help to define a common etiology and range of findings for many of these childhood conditions. Of course, if a child originally was traumatized, one would expect to find vestiges of the repeated visualizations, repeated behaviors and physiologic sensations, specific fears, and revised ideas about people, life, and the future that appear to characterize the childhood traumas.

Denial and Psychic Numbing

Denial and psychic numbing have long been considered classic findings of the posttraumatic stress disorders. Diagnostic problems often arise, however, because massive denial and emotional shutdown are so often evanescent or absent in children who have gone through single shocks (17). Although conscious suppression of thoughts will take place in any kind of trauma, and although brief, limited denial and numbing may last from moments to hours after a shocking event, massive denial and psychic numbing are primarily associated with the long-standing horrors of childhood, what I would call the type II traumas. Children who experience this type of stress may employ such extreme numbing and denial that they look extremely withdrawn or inhuman. When very young, they may assume the guise of Spitz's "hospitalism" babies (33) or of "hail fellow well met" superficiality (34), both of which are signs of failure of attachment and of personality organization.

Children who experience type II traumas do not complain of going "numb." The sense of going dead is one that depends upon years of subjectively knowing what it was to feel alive. On the other hand, children who have been repeatedly brutalized or terrorized *do* exhibit massive denial to the eyes of the trained observer. Such children avoid talking about themselves. They often go for years without saying a thing about their ordeals. They valiantly try to look normal at school, in the neighborhood, and on the playground. They may tell their stories once or twice and entirely deny them later. (This is quite different from some children who have experienced type I traumas, who may tell their stories even at kindergarten Show and Tell.)

Children who experience type II traumas often forget. They may forget whole segments of childhood—from birth to age 9, for instance. Where one sees the difference between these "forgetful" children and ordinary youngsters is in the multiply traumatized child's relative indifference to pain, lack of empathy, failure to define or to acknowledge feelings, and absolute avoidance of psychological intimacy. Repeatedly brutalized, benumbed children employ massive denial—and when their denial-related behaviors cluster together, the resultant childhood personality disorder (one that cuts across adult narcissistic, antisocial, borderline, and avoidant categories) is massive.

Profound psychic numbing in children occurs as an accommodation to the most extreme, long-standing, or repeated traumatic situations. Childhood physical and sexual abuse represent two of these extremes. What still makes the underlying idea of "trauma" the correct etiology and pathogenesis here is the fact that the specific fears, the repeated play, the behavioral and physiologic reenactments, the tendencies toward visualizations, and the revised ideas about life, people, and the future seem to persist in so many of these children for years after the last abuse stops.

Suzanna was 6 years old when her teenaged brother began sexually molesting her. (It turned out that he, in turn, had been sexually molested by a junior high school teacher before he began abusing Suzanna.) Suzanna once tried to tell her mother, "Nobody's supposed to touch you in your—" (she pointed at her genitals). But after that she said nothing further to her parents, teachers, or friends until the school nurse discovered what was happening 2½ years after it began.

On psychiatric examination when she was age 9, Suzanna spent much of the first hour pushing her index finger back and forth through a small hole she had made with the rest of her fingers. She repeatedly rubbed the loose couch pillows over one another. She said of her experiences with her brother, "He put his penis where I pooped. It hurt. I told him it hurt, but he said nuttin' back. I didn't like that at all. It didn't really frighten me. Not really. I just made up my mind to think about other things."

When Suzanna was asked how she was able to do this mind trick, "to think about other things," she replied, "I say 'I don't know' over and over to myself. When I say my prayers I keep saying the last word of the prayer. Sometimes I do it a hundred times. I say 'I don't know' a lot of times in my mind each day. . . . Sometimes now I find myself not feeling things. I don't feel sad or mad when I should be. I'm not afraid when I should be. I act silly and crazy a lot. The people at my school think I'm funny because of it."

Self-Hypnosis and Dissociation

Spontaneous self-hypnosis, depersonalization, and dissociation are important outcomes of repeated, long-standing terrors (the type II traumas). Children who have been the victims of extended periods of terror come to learn that the stressful events will be repeated. Some of these children, the ones, perhaps, who have an innate ease of hypnotizability, spontaneously fall upon the technique of self-hypnosis. This mechanism enables a child mentally to escape. Suzanna, the child described in the previous paragraph, used the repetition of a single word, the last word of her prayers, to accomplish this escape from pain and worry. She also lulled herself into minitrances by saying "I don't know" in her mind. The children at school recognized her affect to be unusual. But nobody but the child herself could recognize the self-hypnosis.

Traumatized children who use a great deal of self-hypnosis may, in fact, go on to develop adult multiple personality disorders (35). This is probably a rare condition. Spontaneous dissociation, however, accounts for a number of more commonly observed findings in abused children—bodily anesthesias, feelings of invisibility, and amnesias for certain periods of childhood life.

Multiple personality disorder, a syndrome in search of its own place in our diagnostic manuals, belongs here, at least in terms of etiology—the repeated, extreme, long-standing traumas of childhood. In children, periods of time that cannot be accounted for, problem behaviors, visual and auditory hallucinations, and headaches appear to indicate that the child is suffering from multiple personality precursors (36). Most self-hypnotizing children who are type II trauma victims fall short of the multiple personality or precursors diagnoses, however. They develop, instead, anesthesias to bodily pain, sexual anesthesias, and extreme emotional distancings. Children who come to expect the repetition of terrors remove themselves in any way that they can. These emotional removals are not possible for the ordinary type I trauma victim.

Frederick was 7 years old when he was sent to live with his aunt because his mother found out, through a tape recording set up to catch her husband at infidelity, that Frederick's stepfather had been throwing him against walls while she worked the evening shift. Frederick did not tell anyone his year-long story, despite two visits to the emergency room and one neighbor-instigated protective service investigation.

While in his aunt's custody, Frederick glanced down at the playground pavement one day and saw blood. After several seconds of searching for a wounded companion, Frederick realized that it was *he* who was bleeding. The boy realized he could feel no pain.

In a psychotherapy session I asked Frederick how he could make this sort of thing happen. "It jus' happens now," he said. "I used to pretend I was at a picnic with my head on Mommy's lap. The first time my stepdaddy hit me, it hurt a lot. But then I found out that I could make myself go on Mommy's lap [in imagination], and Winston couldn't hurt me that way. I kept goin' on Mommy's lap—I didn't have to cry or scream or anything. I could *be* someplace else and not get hurt. I don't know how many times Winston punched me out. I wasn't always payin' attention. Like I told you, first I'd be at a picnic on Mom's lap. Later I didn't have to think of no picnic—jus' her lap. Now if somethin' makes me bleed, I don't think of no lap at all. I jus' don't feel no pain."

Jamie was repeatedly abused by his alcoholic father. He had also repeatedly observed his father beat his mother. At age 8, he witnessed his mother shoot his father to death. When he was 9, the child was psychologically evaluated. At that time he told me, "I started some planets. I made my planets up as a game. But it's real now. It's no game anymore." Jamie described a safe planet he had invented long ago, his own planet. He also had invented a number of very unsafe planets where people "got killed." He said that he had come to achieve invisibility by repeatedly visiting his own safe planet and avoiding the unsafe ones. "Starting when I was 6," he said, "I began to feel invisible. When my Mom pointed a gun at my Dad . . . I was thinking like 'I didn't see it,' like 'This didn't happen.' I blinked to see if I was dreaming. . . . I remember at first pretending I wasn't there—that I didn't see it—that I was on my own planet. I had gone there a lot before. When Mom and Dad would fight, I would try not to hear, not to see. I'd try to go to sleep. Normally I couldn't. I'd try to get out of the room where they were. I'd try to visit my planet. But now my mind, yes, it just goes blank. Mostly it happens at home. A few minutes at a time."

Jamie repeatedly dreamed by night about his father's death. And he visualized the killing by day. But from the moment that his dad was shot, Jamie wondered if he himself could turn invisible. "I know I can," he said. "I do it here on earth. I do it all the time on my planet. You're just going to have to believe me. My friends believe it. . . . When my father was being shot I felt invisible. But if I turned invisible in front of everybody, they'd take away my powers."

Rage

Rage, including anger turned against the self, is a striking finding in those posttraumatic disorders that are brought on by repeated or long-standing abuses, the type II disorders. One observes rage and its negative, extreme passivity, in those type II disorders originating in places where trust originally resided. Dorothy Otnow Lewis and her group reported that among adolescent delinquents who go on to commit murder, chronic physical abuse is a key finding within a cluster of several other key findings (36). The rage of the repeatedly abused child cannot safely be underestimated.

Reenactments of anger may come so frequently in the type II trauma disorders that habitual patterns of aggressiveness are established. The rage may become so fearsome to the child as to create extremes of passivity. Wild fluctuations of both active anger and extreme passivity may so dominate the clinical picture that the young person is eventually given a diagnosis of borderline personality. Defenses against rage such as passive into active and identification with the aggressor also put their own peculiar stamps on the type II child. Type II children have been known to attack their own bodies. Self-mutilations or physically damaging suicide attempts occur. The festering anger of the repeatedly abused child is probably as damaging a part of the condition as is the chronic numbing. Both of these, in fact, the numbing and rage, probably figure later in the antisocial, borderline, narcissistic, and multiple personality diagnoses that are so often part of the picture of the type II traumatized child grown up.

A 5-year-old boy whose new stepmother had been tying him with ropes and leaving him locked up in closets behaved well at kindergarten. At home, however, he took scissors to his stepmother's best lingerie. He sprinkled India ink twice into the family wash. He consistently managed not to eat the food his stepmother prepared for him. The boy's stepmother said he was asking for the punishments she gave him. And so the abuses escalated.

A 45-year-old woman had been a teenager in summer camp when the atomic bomb destroyed her home in Hiroshima. (Her immediate family was spared; all were out of town on Aug. 6, 1945.) As an adult, the woman could not get along well with her American-born husband, alternately accusing him of laziness, ineptitude at work, and infidelity. From the time her daughter turned 13, the woman began believing the girl to be promiscuous, a liar, a drug addict, and a thief. The woman could not get along with her co-workers at the international law office where she worked. She was able, she said, to relate only to customers from Japan. They reminded her "of the people [she] used to know at home when [she] was a girl." I invited the woman to come to my office to talk about her experiences with the bomb. She made two appointments for this purpose but failed to appear for either. Obviously, too much time had elapsed to prove any cause-and-effect hypothesis here. It is interesting, however, that the woman's anger and suspiciousness rested only with American and American-influenced people. Native Japanese persons, the victims, not the perpetrators of the atomic bomb, were entirely spared her wrath.

CROSSOVER TYPE I-TYPE II TRAUMATIC CONDITIONS OF CHILDHOOD

When a single psychological shock takes a child's parent's life, leaves a child homeless, handicapped, or disfigured, or causes a child to undergo prolonged hospitalization and pain, the ongoing stresses tend to push the changes in the child toward those characteristic of the type II childhood traumas. In these cases one often finds features of both the type I and the type II conditions. Those children with permanent handicaps, longstanding pain, or loss of significant objects are often forced into making significant character changes or using numbing tricks to minimize their pain. They may still retain, however, the characteristics typical of responses to single events—clear memory, perceptual distortions, and omens.

Perpetual Mourning and Depression

Psychic shock interferes with childhood bereavement and vice versa (37). The combined psychological effects of shock and grief continue to drag on throughout childhood. As time goes by, and the childhood mourning does not proceed through its ordinary stages (38), the young trauma victim is reinjured—from the inside this time—through prolonged exposure to sadness and loss. The psychological condition of mixed mourning and trauma in youth may take the guise of major affective disorder and may have to be treated as such, at least at first. There is a high rate of depression in refugee children from brutal regimes (15, 16). An explanation for this finding may be the unresolved trauma that potentiates and extends the unresolved grief, the grief that furthers the trauma, or both.

A 4-year-old boy watched his older sister's evisceration in a freak accident in a children's swimming pool. Before the disaster she had asked him to play, but he had refused. The little girl then sat down on an exposed drain pipe. The boy spent a couple of years after the accident using wooden blocks to build his own perfect pool. He blamed himself for not agreeing to play with his sister, an act, he felt, that caused his sister's injury. The boy retained a clear memory of all of the events. He showed symptoms typical of type I trauma.

Following his sister's death in transplantation surgery 2 years after the accident, the boy began to retreat from his friends, avoid participating in class, and stay silent much of the time. His teachers complained about his extreme passivity and said he was losing ground in subjects in which he had already proved himself. He lost some weight and stopped sleeping through the night. He lost his playfulness and began losing his friends. His 2 years of mourning had introduced type II characteristics into a previously pure type I disorder.

Childhood Disfigurement, Disability, and Pain

Children who are physically injured in psychically traumatic accidents tend perpetually to mourn old selves, personas that were previously intact and perfect. Even when perpetual grief is not the problem, posttraumatic physical handicaps frequently demand considerable personality reorganization in order that the child can live with a new, limited self. In children, character rearrangements may become massive. To deal with the pain and procedures accompanying traumatic accidents, children may employ self-hypnosis. They may experience self-revulsion, unremitting guilt and shame, impotent rage at their peers who shun and tease them, and sadness. Suicide attempts are not infrequent in this group. Robert Stoller suggested in a recent paper that some extremes of adult sadomasochistic behavior may originate in painful illnesses, injuries, and procedures during childhood. Rather than self-hypnotizing, these children may divert themselves from the pain by self-stimulating—and thus perpetually associate their pain with sexuality (39). Childhood syndromes of injury and shock do not consistently qualify, under *DSM-III-R* criteria, as posttraumatic stress disorders (40). But these mixed syndromes of depression, numbing, rage, and fright often carry many of the four characteristics that I associate with childhood traumas. Adjustment to a sudden surprise, coupled with a prolonged ordeal, often lies at the origin of the problem.

A kindergartner climbed onto a large department store display table, causing it to fall over onto her face as her grandmother paid the clerk for a purchase. The child's facial bones were smashed, and although they were beautifully reconstructed, she looked quite different than she had before the accident. Old friends did not recognize her, and other kindergartners told the child that she must be pretending to be Belinda—she could not actually *be* Belinda.

The little girl, previously outgoing, mischievous, and vivacious, took on a quiet, remote, and perfectly well-behaved mode of behavior. Two years after the accident she said, "I was a devil before, but I was punished for it. Now I'm good." Despite the fact that she experienced bad dreams, liked to play alone under chairs, and tended to mutilate her dolls' faces, Belinda's character change dominated all other posttraumatic findings.

SUMMARY

There appears to be a group of problems brought on in childhood by the experience of extreme fright generated by outside events. Some of these childhood problems are created by one external shock, and others are created by a multiplicity of blows. Untreated, all but the mildest of the childhood traumas last for years. The child's responses, in fact, may create a number of different kinds of problems in adult life. There are four characteristics, however, that seem to affect almost everyone subjected to extreme terrors in childhood. These findings seem to last and can be retrieved in histories. They include repeated visualizations or other returning perceptions, repeated behaviors and bodily responses, trauma-specific fears, and revised ideas about people, life, and the future. These four findings appear to remain clustered together in childhood trauma victims even when other diagnoses seem more appropriate. Like rheumatic fever, childhood trauma creates changes that may eventually lead to a number of different diagnoses. But also like rheumatic fever, childhood trauma must always be kept in mind as a possible underlying mechanism when these various conditions appear.

If one takes all of the disorders of childhood brought on by extreme external events and puts them into the general category of trauma, they can be roughly subdivided into two groupings: type I, which is brought on by one sudden shock, and type II, which is precipitated by a series of external blows. Crossover conditions are quite common and develop when one blow creates a long-standing series of childhood adversities.

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A Prospective Comparison of Four Insanity Defense Standards

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Objective: Controversy about the formulation of the insanity defense has been intense, but little empirical work is available regarding how different standards affect court findings. The major aims of the present study were to determine if different standards for determining insanity produced different judgments and to provide a broad descriptive picture of those cases in which the standards appeared to make a difference. Method: Four forensic psychiatrists were asked to indicate whether they thought 164 defendants met any or all of four insanity tests: 1) the American Law Institute (ALI) cognitive criterion, 2) the ALI volitional criterion, 3) the APA test, and 4) the M'Naghten rule. Results: The four psychiatrists determined that 97.5% of the defendants met the ALI volitional criterion, 73.9% met the APA criterion, 70.3% met the M'Naghten rule, and 69.5% met the ALI cognitive criterion. Nearly two-thirds of the defendants met all four insanity tests, and 24.4% met only the ALI volitional test. Few defendants met cognitive tests without also meeting the ALI volitional test. Elimination of the volitional test for insanity reduced the rate of psychiatric recommendations of acquittal by 24.4%. Conclusions: These findings highlight the fact that the primary logical division between volitional and cognitive standards appears to be powerful but that distinctions between types of cognitive standards are not terribly powerful. In addition, the variation among individual raters must be viewed as an important determinant of how any insanity standard is applied.

(Am J Psychiatry 1991; 148:21–27)

For the last century, sporadic yet heated debate has occurred in the United States about the reasonableness of the legal defense of insanity for a criminal charge (1–4). Controversy has intensified in recent years, with recurrent legislative attempts at the state and federal levels to modify or abolish statutory language regarding the insanity defense. Responding to this furor, APA recommended that exculpation by mental disease or defect should occur on the basis of an impairment of cognitive capacity rather than of cognitive or volitional incapacity (5). It cited and approved Bonnie's proposal ("A person charged with a criminal offense should be found not guilty by reason of insanity if it is shown that as a result of mental disease or mental retardation he was unable to appreciate the wrongfulness of his conduct at the time of the offense" [6]).

The APA cognitive test, like the M'Naghten rule, eliminates the volitional component of the American Law Institute (ALI) formulation used in nearly half of the states (7). While advocating such a cognitive test,

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APA also acknowledged some uncertainty about its effect because the wording of the insanity defense has not been demonstrated to be the predominant factor in determining whether a defendant is acquitted by reason of insanity (2, 3). Nevertheless, Congress adopted this insanity defense standard following the acquittal of John Hinckley (8–10).

Little empirical work is available regarding how different standards affect whether defendants are found to meet the requirements for an insanity defense. Both Congress and APA have been sharply criticized for their decisions given the current paucity of research support for such a change (11–13). Much of the available empirical information approaches the subject indirectly.

Several studies have reported changes in the rate of insanity acquittals following alterations in the applicable insanity test. In the District of Columbia, following the 1954 implementation of the Durham rule (a defendant is exculpated when his or her conduct was the product of a mental disease or defect) (14), there was a marked increase in the number of defendants who were acquitted by reason of insanity until 1963, when the acquittals sharply declined (15, 16). In Oregon (17), insanity acquittals increased tenfold after the ALI standard replaced the M'Naghten rule. In California (18), insanity acquittals sharply increased following the adoption of the ALI rule in 1978 and then decreased following the return of the M'Naghten rule. Similarly, a change in the insanity rule from the M'Naghten (1965 to 1966) to the ALI (1972 to 1973) standard in Maryland (19) paralleled an increase in psychiatric judgments of defendants as insane (as opposed to actual acquittals) from 7.9% to 19.2%.

In contrast to these findings, Pasewark et al. (20) found that Wyoming's change from M'Naghten plus the irresistible impulse test (1970 to 1972) to the ALI test (1975 to 1977) effected no change in the proportion of defendants found legally insane. Packer (21) also found no significant change in the number of insanity acquittals in Michigan after that state adopted the ALI rule in 1975; unfortunately, other statutory changes involving the definition of mental illness for the purpose of criminal insanity as well as the administration of the insanity defense were also implemented at that time, precluding the identification of any causal relationship. The uncontrolled nature of this general line of investigation renders suspect any conclusions about the relationship between statutory criteria for insanity and psychiatric recommendations or legal adjudications of criminal responsibility.

Simon (3) studied decision making by juries and jurors using different insanity tests. Individual mock jurors and mock juries who heard a recording of a defendant's trial on a charge of incest showed a nonsignificant trend to vote for insanity acquittal when they were instructed under the Durham rule (36% acquittals by jurors, 19% acquittals by juries) than under the M'Naghten rule (24% acquittals by jurors, no acquittals by juries). No significant differences in acquittal rates based on the two insanity tests were obtained for trials conducted on a charge of housebreaking, but the investigator identified methodological weaknesses in this phase of the experiment. Forty-nine percent of her jurors thought the Durham rule was more favorable to defendants, 19% thought M'Naghten was more favorable to defendants, and 32% viewed the two tests as equally favorable to defendants. Another mock juror study (22), using college students, written hypothetical cases, and six insanity tests, found no significant difference in acquittal judgments with the different insanity tests.

Silver and Spodak (23) provided the only empirical attempt to evaluate the scope of different insanity standards at one time. In their retrospective study, nine experienced forensic psychiatrists reviewed the records of 42 defendants who previously had been evaluated as inpatients and reported to the criminal court as not responsible for their alleged crimes by reason of insanity. The original criminal responsibility evaluations had been conducted as composite evaluations by at least three staff psychiatrists. The report to the court listed psychiatric observations, diagnoses, and opinions on criminal responsibility but did not cite which insanity criterion (volitional versus cognitive) was the basis for the final composite opinion.

By reviewing the case files of the 42 defendants, Silver and Spodak's nine psychiatrists attempted to determine retrospectively which ALI criterion—volition or cognition—the defendants appeared to meet. Of the 117 criminal responsibility opinions, only 22% rested on one ALI criterion. Almost 13% of the insanity opinions were based solely on the ALI cognitive test. There was considerable variation among the psychiatrists in this regard; the frequency with which their opinions were based on a single criterion rather than dual ALI criteria ranged from 0% to 43%. The remainder of criminal responsibility opinions, with one exception, were based on both ALI criteria. Because of the composite nature of the final judgment, hypothetical elimination of the ALI volitional test converted two (5.1%) of 39 cases from not responsible to criminally responsible. In addition, eliminating the volitional test changed composite opinions of not responsible that were unanimous among the raters to composite opinions of the majority in only 11 (28.2%) of 39 cases. Thus, a paradoxical increase in the frequency of contested insanity cases could occur by excluding the ALI volitional standard. Questions about the validity of such methods, however, limit the generalizability of these results.

In the present study we investigated in a prospective manner whether different insanity defense standards affected forensic psychiatrists' opinions of defendants' criminal responsibility. Experienced psychiatrists judged actual cases using multiple standards. The major aims of the study were twofold: 1) to determine if the different standards really produced different judgments in a sizable number of cases and 2) to provide a broad descriptive picture of those cases in which the standards appeared to make a difference.

METHOD

The legal insanity judgments of four full-time forensic psychiatrists who were employed by the court clinic of a large Midwestern city were examined in this investigation. All four psychiatrists were certified by the American Board of Psychiatry and Neurology, Inc. The clinic provides pretrial psychiatric evaluations of criminal defendants at the request of the court, state's attorney, or defense attorney without cost to the defendant. Social and family history data as well as psychological testing information are provided in writing to the psychiatric evaluator by the clinic's psychologists and social workers. Psychiatric reports on criminal responsibility are then prepared by each psychiatrist after one or more personal interviews with the defendant. Each of the psychiatrists formulates an opinion about criminal responsibility independently; this opinion is available to the court and to prosecuting and defense attorneys for review. The psychiatrist provides testimony in court on request. Informed consent for their participation in this research was obtained from each psychiatrist.

Each of the psychiatrists completed a one-page questionnaire when he gave an opinion that a defendant met the state's statutorily defined criteria for not guilty by reason of insanity. During the period of this study, and for many years before it, the ALI criminal responsibility criteria, which allow for the use of either a volitional or a cognitive standard, were used in this jurisdiction. These criteria state, "A person is not criminally responsible for conduct if at the time of such conduct, as a result of mental disease or mental defect, he lacks substantial capacity either to appreciate the criminality of his conduct or to conform his conduct to the requirement of law." The psychiatrists did not complete the questionnaire if they gave the opinion that the defendant was criminally responsible for the offense.

Each psychiatrist was asked to identify himself on the questionnaire and then to identify the age, sex, race, number of years of school completed, criminal charges, and *DSM-III* diagnoses of the defendant. The psychiatrist also indicated whether, in his opinion, the defendant met any or all of four distinct insanity tests with regard to the alleged criminal offense: 1) the ALI cognitive criterion (Because of mental disease or defect, did the defendant lack substantial capacity to appreciate the criminality of his conduct?), 2) the ALI volitional criterion (Because of mental disease or defect, did the defendant lack substantial capacity to conform his conduct to the requirements of the law?), 3) the APA test (Because of mental disease or mental retardation, was the defendant unable to appreciate the criminality of his conduct at the time of his offense?), and 4) the M'Naghten rule (At the time of the act, was the defendant laboring under such a defect of reason, from disease of the mind, as not to know the nature and quality of the act he was doing; or if he did know it, that he did not know he was doing what was wrong?).

TABLE 1. Most Serious Crimina Charge for 164 Defendants Recommended by Four Psychiatrists to Be Not Guilty by Reason of Insanity

Charge	N	%
Murder	21	12.8
Attempted murder	31	18.9
Solicitation to murder	1	0.6
Rape	3	1.8
Attempted rape	1	0.6
Deviate sexual assault	1	0.6
Attempted deviate sexual assault	1	0.6
Armed robbery and attempted armed robbery	3	1.8
Robbery and armed violence	7	4.3
Aggravated arson	15	9.1
Arson	6	3.7
Indecent liberties with a child	2	1.2
Aggravated kidnapping, kidnapping	4	2.4
Aggravated battery	22	13.4
Unlawful restraint	2	1.2
Intimidation	1	0.6
Burglary and attempted burglary	14	8.5
Home invasion	1	0.6
Auto theft	3	1.8
Theft	10	6.1
Criminal damage to property	2	1.2
Unlawful use of a weapon	1	0.6
Aggravated criminal sexual assault	5	3.0
Attempted criminal sexual assault	1	0.6
Threatening a public official	1	0.6
Disorderly conduct	1	0.6
Eavesdropping	1	0.6
Heinous behavior	1	0.6
Missing data	2	1.2

TABLE 2. Principal Axis I *DSM-III* Diagnosis for 164 Defendants Recommended by Four Psychiatrists to Be Not Guilty by Reason of Insanity

Principal Axis I Diagnosis	N	%
Schizophrenic disorder	84	51.2
Schizoaffective disorder	21	12.8
Paranoia	10	6.1
Major depression	2	1.2
Bipolar disorder	17	10.4
Atypical psychosis	4	2.4
Primary degenerative dementia	3	1.8
Organic delusional syndrome	1	0.6
Organic personality syndrome	1	0.6
Organic brain syndrome	7	4.3
Mental retardation	10	6.1
Alcohol hallucinosis	1	0.6
Alcohol abuse	1	0.6
Chronic posttraumatic stress disorder	1	0.6
Atypical dissociative disorder	1	0.6

In addition, the psychiatrist reported his degree of certainty in each of the four assessments on a scale of 0% to 100%. Legal outcome of the case was later obtained when possible to determine whether the defendant was adjudicated guilty, not guilty, not guilty

TABLE 3. Judgments and Confidence in Their Judgments of Four Psychiatrists on Whether 158 Defendants Met Four Tests of Insanity

	Yes[a]				No[c]			
			Rating of Confidence in Their Judgment (%)[b]				Rating of Confidence in Their Judgment (%)[b]	
Insanity Test	N	%	Mean	SD	N	%	Mean	SD
ALI cognitive test	109	69.0	81.7	16.4	49	31.0	68.8	13.6
ALI volitional test	154	97.5	83.9	11.9	4	2.5	78.8	20.2
APA standard	116	73.4	80.7	16.6	42	26.6	70.4	13.0
M'Naghten test	111	70.3	81.7	16.8	47	29.7	68.3	14.8

[a] The examiner rated the defendant as meeting this test.
[b] The psychiatrists were asked to rate their confidence in their judgments from 0% to 100%.
[c] The examiner rated the defendant as failing this test.

TABLE 4. Combinations of Recommendations Made by Four Psychiatrists According to Four Tests of Insanity for 164 Defendants[a]

Combination of Insanity Test Recommendations[b]	Defendants	
	N	%
Yes by ALI cognitive, ALI volitional, APA, and M'Naghten	103	62.8
No by ALI cognitive, yes by ALI volitional, no by APA, no by M'Naghten	40	24.4
No by ALI cognitive, yes by ALI volitional, yes by APA, no by M'Naghten	6	3.7
Yes by ALI cognitive, yes by ALI volitional, yes by APA, no by M'Naghten	1	0.6
Yes by ALI cognitive, no by ALI volitional, yes by APA, yes by M'Naghten	4	2.4
No by ALI cognitive, yes by ALI volitional, yes by APA, yes by M'Naghten	2	1.2
Yes by ALI cognitive, yes by ALI volitional, no by APA, yes by M'Naghten	1	0.6
No by ALI cognitive, yes by ALI volitional, no by APA, yes by M'Naghten	1	0.6

[a] Data were missing for six subjects.
[b] Yes indicates that the examiner rated the defendant as meeting this test. No indicates that the examiner rated the defendant as failing this test.

by reason of insanity, or guilty but mentally ill by the judge or jury. By design, no specific training in the application of the insanity tests was provided to the psychiatrists because they were experienced forensic practitioners and we were interested in the actual use of the insanity tests in practice.

The statistical tests used to analyze the data included chi-square tests, t tests, Pearson pairwise binary correlations, and repeated-measures multivariate analysis of variance (MANOVA).

RESULTS

Defendant Sample

Consecutive criminal responsibility evaluations performed over a 2-year period (1984 and 1985) by the four psychiatrists were examined. Only evaluations in which the psychiatrist initially gave the opinion that the defendant met the ALI insanity criteria (ALI volitional, ALI cognitive, or both) were included in the sample. The total number of evaluations performed during the study period in which the study psychiatrists reached this conclusion was 205. Forty-one of the evaluations were done for the same defendants, so only first-time evaluations of defendants were used in the present study, resulting in 164 evaluations.

Of the 164 defendants examined and thought to have met the criteria for an insanity defense, 139 (84.8%) were men and 25 (15.2%) were women; 95 (57.9%) were black, 64 (39.0%) were white, four (2.4%) were of other races, and data were missing for one (0.6%). The mean±SD age of the defendants was 34.4±12.7 years, with a range of 18 to 78 years.

The most serious pending criminal charges for the defendants are shown in table 1. Of note is that 52 (31.7%) of the defendants were being held on charges of property crimes. The defendants' principal *DSM-III* axis I diagnoses at the time of the evaluation are presented in table 2.

Insanity Recommendations

Complete data regarding raters' levels of confidence were available for 158 of the 164 cases. Table 3 shows the psychiatrists' recommendations on the insanity defense and the amount of confidence they had in their judgments for each insanity test. According to these four forensic psychiatrists, the overwhelming majority of the evaluated defendants met the criteria for the ALI volitional test; fewer were judged as meeting the other three tests. As expected, the ALI volitional test proved open to considerably broader applicability than the other tests.

Table 4 shows the frequency with which the forensic psychiatrists endorsed the different insanity tests. Nearly two-thirds (62.8%) of the defendants were evaluated as meeting all four insanity tests. Approximately one-quarter (24.4%) were evaluated as meeting only the ALI volitional test. Defendants who met other insanity test criteria comprised 9.1% of the sample, and data were missing for 3.7%. These regularities show clearly that, in a substantial number of cases, the difference between the ALI volitional test and the other

TABLE 5. Pearson Pairwise Binary Correlations of Insanity Standards Applied by Four Psychiatrists to 164 Defendants

Test	ALI Cognitive Test		ALI Volitional Test		APA Test		M'Naghten Test	
	r	p	r	p	r	p	r	p
ALI cognitive test	—	—	−0.106	≤0.089	0.432	≤0.000	0.941	≤0.000
ALI volitional test	—	—	—	—	−0.048	≤0.272	−0.105	≤0.095
APA test	—	—	—	—	—	—	0.862	≤0.000
M'Naghten test	—	—	—	—	—	—	—	—

insanity tests was clearly distinguishable to these psychiatrists.

When examined with chi-square or t tests when appropriate, there were no significant (with p set at 0.05) differences in age, race, sex, charge, or diagnosis among the defendants meeting the different patterns of insanity standards (collapsed into the endorsement of all standards, only the ALI volitional standard, or some other combination of standards). However, the psychiatrists showed significant variation in their tendency to choose among these patterns ($\chi^2=35.21$, df=6, $p\leq0.001$). Regarding the ALI volitional standard alone, for instance, the four psychiatrists chose this alternative five (7.8%) of 64 times, five (15.2%) of 33 times, seven (25.9%) of 27 times, and 23 (57.5%) of 40 times, respectively. If the low or high users of this alternative alone are eliminated from the analysis, the estimates for the reliance of psychiatrists on the volitional test alone ranged from 15% to 26%.

An examination of the Pearson pairwise binary correlations of the endorsements of the four different standards showed clearly how the examiners saw the interrelationships among these standards. As shown in table 5, the M'Naghten standard was highly related to both the ALI cognitive standard and the APA standard. The ALI cognitive standard and the APA standard were somewhat less closely related. The ALI volitional standard, meanwhile, was the clear outlier of the four, showing no statistically significant relationship to any of the other three.

Examiner Confidence

The psychiatrists' confidence in their choices of each alternative could be attributed to several factors, such as the psychiatric examiner's overall level of confidence, the differing levels of confidence attached to the choice of an affirmative or a negative response, and the level of confidence that can be attached to the choice of each insanity test. Table 3 shows the psychiatrists' mean levels of confidence in their judgments based on each insanity test, separating examiners' affirmative from negative responses for each test outcome. For all the tests, examiners were more confident in indicating that a defendant met the criteria than that a defendant did not. Also, when the psychiatrists' mean levels of confidence in their judgments were examined without regard for whether an affirmative or negative response was given, it was clear that the psychiatrists' confidence in their judgments based on the ALI volitional test exceeded that for judgments based on each of the other three tests.

Directly testing the variation in the psychiatrists' levels of confidence in their judgments based on the different standards, taking into account the examiner and the type of response (affirmative or negative), presented a difficult analytic task. Each psychiatrist gave four responses, one for each standard, producing a within-subjects repeated measure. Also, the type of response was not really crossed with the examiner but, instead, nested within the examiners because each provided a different proportion of affirmative and negative responses. To address this design, we conducted a repeated-measures MANOVA with the four confidence scores as dependent variables, the examiner as an independent variable, and response type as an independent variable nested within examiner. Complete data regarding raters' levels of confidence were available for 158 of the 164 cases.

This analysis showed a significant main effect for the type of standard (F=6.02, df=3, 471, $p\leq0.001$), a significant main effect for the examiner (F=4.01, df=3, 155, $p\leq0.009$), and a significant Examiner by Standard interaction (F=2.20, df=9, 465, $p\leq0.02$). Examination of the univariate tests related to response type showed a significant main effect for this variable on the ALI cognitive standard (81.3%–68.9%) (F=5.68, df=4, 155, $p\leq0.001$) and the M'Naghten standard (81.7%–68.3%) (F=3.70, df=3, 156, $p\leq0.01$). The variation in confidence ratings thus appears to be related to which psychiatrist was making that determination and which standard he was using. For the ALI and M'Naghten standards, whether the psychiatrist was deciding that the person met or did not meet the standard in question also appears to be important.

Legal Outcome

Due to time delays in bringing criminal cases to trial in this jurisdiction and the difficulty of collecting periodic follow-up data, information on the legal outcome of the case was missing for 52 (31.7%) of the 164 cases. In the 112 cases for which data were available, 91 (81.3%) were found not guilty by reason of insanity, 11 (9.8%) were found guilty, seven (6.3%) were found not guilty, and three (2.7%) were found guilty but mentally ill or had another disposition. Unfortunately, the large amount of missing information on this variable made it unwise to pursue investigation of the relationships between the rating psychiatrists' judgments and the eventual legal outcome.

DISCUSSION

Although direct empirical data on psychiatric decision making in regard to the insanity defense have been sparse, the results of Silver and Spodak (23) are worth noting in relation to our present findings. Those authors reported a nonsignificant finding that 13% of individual examiners' opinions were based solely on the ALI volitional criterion. Unfortunately, because of the retrospective method used, it is questionable whether this figure can be taken as an accurate estimate of the effect produced by elimination of this insanity standard because one would expect less of an effect in a prospective study than in a retrospective study. To our knowledge, this study provides the only readily available idea of how dependent the decisions regarding patients in insanity defenses are on different standards.

The present study reveals a slightly different, and fuller, picture of the role of insanity standards in the formulation of psychiatric recommendations. Examiners in the present investigation prospectively reviewed different defendants, and most recommended acquittal on the basis of both ALI insanity criteria. Almost all defendants met the volitional criterion, and two-thirds also met any or all of the other three criteria, each generally identified as essentially cognitive in type.

Two predominant patterns emerged from the data: defendants who were said to meet all insanity tests (62.8% of the defendants) and defendants who met only the ALI volitional criterion (24.4%). Together, these two groups comprised 87.2% of evaluated defendants. Only four defendants met cognitive test criteria without meeting the volitional criterion. Thus, on the basis of these data, one could expect elimination of the ALI volitional criterion to reduce acquittal by reason of insanity recommendations by a margin considerably higher than Silver and Spodak postulated (24% instead of 13%).

Considerable variation in the use of the ALI volitional standard existed among the examiners, but even an adjusted estimate of its importance using only the three psychiatrists who made less use of this standard showed it to be the pivotal standard in 13.7% of the cases. It is likely, therefore, that the importance of this standard for affecting psychiatric recommendations is underestimated. Such data are contrary to earlier claims in the literature that few defendants meet the volitional criterion without meeting cognitive criteria (24).

A second clear finding is that the cognitive tests appear interchangeable according to these data: there is no support for the claim that the ALI cognitive test is broader than the APA test or the M'Naghten rule, or that the APA test is broader than M'Naghten. Use of the word "appreciate" in the ALI cognitive and APA tests, rather than "knowing" in M'Naghten, appears to have little meaning for the clinical rater. There thus appears to be no empirical difference among the "lack of substantial capacity to appreciate criminality" under the ALI cognitive criterion, the "inability to appreciate criminality" under the APA test, and the failure to "know the nature and quality of the act" or that what he was doing was "wrong" under the M'Naghten rule.

Two other findings are worth reviewing. First, surprisingly few defendants were judged to have only cognitive impairment by any of the cognitive tests. Defendants with cognitive impairment were almost uniformly judged to have volitional impairment as well. This compares with the 8.5% of defendants who were judged insane on the basis of the ALI cognitive criterion in the Silver and Spodak report (23). In addition, it should be noted that confidence in one's use of a standard also proved susceptible to significant variation from rater to rater and from test to test.

In the end, this investigation sheds light on two major issues. First, it highlights the fact that the primary logical division between the volitional and cognitive standards appears to be powerful but that distinctions between types of cognitive standards are not terribly powerful. Second, the variation among individual raters is considerable and must be thought of as an important determinant of how any insanity standard is applied. Another study of a larger sample of evaluators might produce a similar degree of intersubject variation and a similar insanity defense profile, but this cannot be determined from the present data.

Finally, clinical judgments in criminal responsibility may reflect other concerns, such as evaluators' political ideology, profession, personal views about the insanity defense, or concern about the outcome of such judgments, all of which potentially limit the influence of such legal changes (25–27). Although there is high concordance between evaluators and triers of fact on insanity under at least some circumstances (28–30), and evaluators' recommendations about defendants' insanity are the strongest predictors of insanity adjudication (31, 32), an intended narrowing of insanity defense criteria does not necessarily mean that acquittals would in fact decrease in the precise magnitude projected from these data, since evaluators, judges, and juries may effectively increase the scope of the remaining cognitive criteria. We need to know much more about the empirical effect of statutory language on insanity adjudications before intelligent recommendations can be offered in this area by APA or other groups.

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New Policy of Structured Abstracts

Effective with the January 1991 issue, *The American Journal of Psychiatry* will institute a policy of structured abstracts for Special Articles and Regular Articles. Authors of review articles must include the following information, under the headings indicated: *Objective*—the primary purpose of the review article; *Method*—data sources, study selection (the number of studies selected for review and how they were selected), data extraction (rules for abstracting data and how they were applied); *Results*—methods of data synthesis, key findings; and *Conclusions*—including potential applications and research needs. Authors of research articles must include *Objective*—questions addressed by the study; *Method*—design of the study, setting (location and level of clinical care), patients or participants (manner of selection and number who entered and completed the study), interventions (if any), main outcome measures (primary study outcome measure as planned before data collection); *Results*—key findings; and *Conclusions*—including direct clinical applications. Other types of articles, including Clinical and Research Reports, should include unstructured abstracts. Also effective with the January 1991 issue, the maximum number of words for abstracts for Special Articles and Regular Articles will be increased to 250 and for Clinical and Research Reports to 60.

Decision Making in Psychiatric Civil Commitment: An Experimental Analysis

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Susan E. Dickens, M.A., and Michiko Nohara, B.Sc.

Objective: *Legislation in Canada and the United States that was intended to decrease the use of civil commitment has resulted in a paradoxical increase in involuntary hospital admissions. To elucidate the reasons for this increase, this study was designed to assess the relative importance of various factors involved in the decision to commit a patient.* Method: *All psychiatrists in Ontario were sent a questionnaire asking them to make commitment decisions based on hypothetical case vignettes. Four factors were systematically varied in the vignettes: the patients' legal commitability, clinical treatability, alternative resources, and psychotic symptoms. Completed questionnaires, with three vignettes each, were returned by 495 respondents.* Results: *All four variables were statistically significant in the expected direction; legal commitability (i.e., dangerousness to self and/or others, inability to care for self) and presence of psychotic symptoms accounted for the majority of the variance in the final decision to commit.* Conclusions: *These results suggest that psychiatrists in Ontario rely primarily on legally mandated factors (i.e., psychosis and dangerousness) in making their decisions to commit, although a considerable amount of individual variation is also evident.*

(Am J Psychiatry 1991; 148:28–33)

On Nov. 1, 1978, Ontario's highly controversial Mental Health Amendment Act (Bill 19) went into force. Following legislative trends in other Canadian and American jurisdictions, Bill 19 revised the standing statutes pertaining to the criteria for civil commitment. The legislation specifies that the necessary criteria are the presence of mental disease and evidence of imminent danger to self and/or others, manifested by a clearly indicated and recent threat (or action), or lack of competence for self-care. Bill 19 is representative of North American civil commitment reforms of the 1960s and early 1970s, which, in response to civil libertarian pressure, attempted to specify more concretely those conditions which protect the rights of the individual from overwhelming state or *parens patriae* authority (1, 2). Although there is some disagreement with respect to the legislative intent of Bill 19 (3), most policy makers and investigators concur that the purpose of the dangerousness standard was to restrict the use of civil commitment. Thus, the overall intent of Bill 19, as with the dangerousness standard in many U.S. jurisdictions, was to reduce the number of involuntary hospitalizations (4). Studies investigating the effects of Bill 19, however, have revealed that the legislation has not had its intended effect. Martin and Cheung (5), for example, reported a paradoxical increase in the involuntary admission rate in the first 2 years after the enactment of Bill 19. In two separate studies, Bagby and colleagues have reported similar results. They analyzed rates of involuntary admissions to provincial psychiatric hospitals and psychiatric units of general hospitals for 9 years before and 5 years after the reform and found a statistically significant decrease in the rate of involuntary admissions in the first period after the statutory reform but a steady *increase* in each and every subsequent year (6, 7).

A remarkably similar pattern of involuntary admission rates has been reported in many U.S. jurisdictions where investigators have analyzed the effects of legislative reform that sought to decrease the use of civil commitment. Some of these investigations show that there was an immediate decline in involuntary admissions; for example, this was reported in separate studies for Arkansas (8), Florida (9), Hawaii (10), Kansas (11), Massachusetts (12), Nebraska (13), North Carolina (V.A. Hiday, unpublished manuscript, 1979), and

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Washington State (14) and in nine state jurisdictions evaluated in a comprehensive study by Wanck (4). However, like the province of Ontario, many jurisdictions reported an increase in involuntary admissions in the second and subsequent years after the reform, e.g., Arkansas (8), Hawaii (10), Kansas (11), Nebraska (13), and North Carolina (Hiday manuscript). A close examination of Wanck's data (4) reveals similar reversals in Florida, Pennsylvania, New Mexico, North Dakota, Texas, and Washington. Only two states, Massachusetts and Michigan, have seen sustained decreases (4, 12). Moreover, a paradoxical increase in the rate of civil commitments has been reported in California (15), Minnesota (16), and Pennsylvania (17).

A number of explanations for these curious and provocative results have been offered, including increases in involuntary readmissions (6–8, 13, 15, and Hiday manuscript), changes in the characteristics of the patient population served (6, 7, 17), difficulty in adjusting to the substantive and procedural changes in the statutes (13, 15, and Hiday manuscript), the flexibility and relative inability of specific laws to determine the actual practice of civil commitment (18, 19), and the perceived moral obligation of psychiatrists not to neglect those patients who need treatment but otherwise do not meet the criteria for civil commitment (20, 21).

One important but relatively unexplored area in the civil commitment process that might further elucidate these increases in involuntary admissions is the relative importance of the different variables used in the decision-making process. Theoretically, psychiatrists' decisions to seek commitment should be grounded in the accurate diagnosis of mental disorder and should be congruous with the relevant legal statutes. As pointed out by Thompson and Ager (22), however, these factors are often less effectual than more pragmatic considerations such as availability of beds, treatability of patients, and concern about possible liability. Results from studies examining filed civil commitment certificates in Ontario and several U.S. jurisdictions are, in fact, consistent with the opinion that psychiatrists' decisions to seek commitment may not be founded on relevant legal criteria (23–30).

Recent reviews summarizing investigations of the social and personal characteristics of involuntarily hospitalized patients also seem to support this view. Many variables that have no apparent direct relationship with the legal standards of commitment—for example, age, sex, race, economic resources, marital resources, previous treatment, negative attitude, and education—correlate with commitment status at the same relative level of magnitude as characteristics clearly related to legal criteria for commitment, including suicidal and assaultive behavior (31–33). By contrast, two studies which analyzed the association between clinicians' ratings of legal, social, and interpersonal variables revealed that ratings of the relevant legal criteria carried the greatest weight in predicting their subsequent commitment recommendations (34, 35). More recently, Segal et al. (36) also found dangerousness to be the best predictor of psychiatric decisions to commit. However, they explored dangerousness only in relation to other psychiatric symptoms and did not examine social or interpersonal variables.

Despite their obvious ecological validity, these field studies have been hampered by methodological and interpretative problems. The correlational nature of many of these studies precludes the identification of the causal factors in admission decisions. The significant correlation between commitment status and psychosis, for example, may be interpreted in two ways. On the one hand, it is possible that all psychotic patients are truly dangerous to themselves and others and are therefore more committable than nonpsychotic patients. On the other hand, the presence of psychosis may bias examiners toward finding a patient committable to ensure that a psychotic patient does not go without hospitalization and/or treatment. Further, as Apsler and Bassuk (37) noted, the correlational nature of these studies precludes the determination of the interaction of the various factors in determining the final decision. Finally, most field studies lack objective measurement of patient variables independent of the decision maker involved. Hence, clinicians' ratings of patients' characteristics are often correlated with their own admission decisions.

To circumvent these and other more general problems inherent in conducting field studies, the primary purpose of the present study was to use an experimental method to explore what variables psychiatrists regard as important in making a decision to initiate the commitment process. This approach permits a more direct and interactional examination of the causal relationship between commitment decisions and the more critical variables associated with involuntary hospitalization. More specifically, the commitment decision-making process of psychiatrists was examined by using a series of written case vignettes that systematically varied some of the more important factors which appear to be related to commitment decisions.

METHOD

A series of written hypothetical case vignettes, developed by Thompson and Ager (22), depicting mentally disordered individuals for whom commitment might be sought were modified and served as the experimental stimulus. We generated the vignettes by using the facet method of item construction (38, 39) and specifically designed them to investigate the factors identified in the literature and by interviews with experts in the field as critical to civil commitment decision making. Four factors were systematically varied in each vignette: legal standard (six levels), clinical treatability, and alternative resources and psychotic symptoms, each with two levels (high and low). The legal standard factor corresponds to the three legal criteria for commitment in Ontario, each with two levels (high and low), producing six levels overall (i.e., high dangerousness to others, low dangerousness to others, high dangerousness to self, low dangerousness to self, high inability to care for self, and low inability to care for self). High dangerousness to self was indicated by active suicide attempts or plans. Low dangerousness to self was represented by suicidal ideation with no indication of attempts or plans. Similarly, high dangerousness to others was indicated by active attempts or plans to harm others, and low dangerousness to others was represented by thoughts about harming others but without action or plans. High inability to care for self was represented by lack of self-care resulting in serious self-harm, while low inability to care for self was represented by lack of self-care that did not result in serious self-harm. Clinical treatability referred to how treatable the individual was, with previously successful admissions considered to indicate high treatability. An older person with relatively unsuccessful previous hospitalizations was considered to be a low-treatability case. Alternative resources referred to the individual's social and financial resources. A person with a high level of alternative resources was defined as a married, employed individual with a supportive family; a person with a low level of alternative resources was defined as single and unemployed, with an unsupportive family. Psychotic characteristics referred to the presence or absence of psychotic symptoms and insight about need for treatment. High psychosis was defined as presence of psychotic symptoms with no insight; low psychosis was defined as the absence of psychotic symptoms with good insight. The final design was a $6 \times 2 \times 2 \times 2$ between-subjects design, creating a total of 48 different vignettes.

The standard format for constructing the hypothetical case vignettes was as follows.

> A [age greater or less than 30]-year-old [single/married man/woman] is detained for emergency psychiatric evaluation. Subsequent interview and mental status examination reveal that [symptoms described, including manipulation of commitability (i.e., legal standards) and psychosis facets, high and low]. The [man/woman] has had [one/five] previous involuntary hospitalization(s) for similar problems with [good/little] alleviation of symptoms as a result of hospitalization. Currently [he/she is/is not] employed. [His/her] family is [supportive and wish to help in any way they can/unwilling to become involved in his/her treatment]. [He/she] refuses voluntary inpatient hospitalization, stating that [he/she doesn't have any emotional problems/would rather talk about his/her problems to someone as an outpatient and has made a follow-up appointment].

The vignettes have been validated through extensive pilot testing (22) and have been rated as clear, consistent, and believable. Further, the vignettes have been generally identified by raters as successfully manipulating each of the variables (22).

The commitment decision questions (the dependent variables in the study) were formulated to coincide with Ontario civil commitment procedures. In Ontario, civil commitment decisions are left entirely to the discretion of physicians. There are no judicial commitments, although review boards and legal counsel are available for longer-term commitments. Unlike many state jurisdictions in the United States, nonmedical mental health personnel such as nurses, psychologists, and social workers do not have the legal prerogative to file an application for involuntary hospitalization. Procedurally, the first stage in the commitment process is the Application for Psychiatric Assessment, which may be completed by one physician who has personally examined a person within the preceding 7 days and has formed the opinion that the person meets the criteria for involuntary hospitalization. The application is sufficient authority for the patient to be detained, restrained, observed, and examined for up to 72 hours. It does not give authority to treat, even with substitute consent. The next stage, if necessary, is the Certificate of Involuntary Hospitalization, which is used to continue the involuntary hospitalization within 72 hours of the admission of the patient on an Application for Psychiatric Assessment. The certificate must be completed by a different physician than the one who completed the application. The criteria for the certificate are the same as for the application. There need not be ongoing evidence for threats of or actual dangerous behavior toward self or others while the patient has been in the hospital. The Certificate of Involuntary Hospitalization is good for 14 days and can be initially renewed for 1 month. Subsequent renewals are valid first for 2 months and then for 3-month periods.

In accordance with this commitment procedure, the respondents were asked if they would involuntarily hospitalize the person depicted in the vignette for a 72-hour period (Application for Psychiatric Assessment) and how strongly they believed the individual needed hospitalization, according to a 7-point Likert scale (1=definitely does not require hospitalization and 7=definitely does require hospitalization). Second, respondents were asked whether, if the person had already been admitted on an application and his or her status had not changed in 72 hours, they would hospitalize the patient for a further period of up to 14 days (Certificate of Involuntary Hospitalization) and how strongly they believed that the individual required continued hospitalization, according to a 7-point Likert scale.

Three vignettes randomly selected from the pool of 48, a cover letter, a general information sheet, and questions regarding the vignettes were mailed to the entire population of psychiatrists in Ontario. The names were selected from the Ontario section of the 1988 Canadian Medical Directory. A postcard addressed to the researchers was also enclosed. This postcard could be returned under separate cover from the questionnaire. This allowed the participants to indicate, anonymously, whether they had responded and indicated to the researchers who should receive a second mailing.

RESULTS

A total of 1,251 questionnaires were mailed out. If a response was not received 2 weeks after the first mailing, a second questionnaire was sent. Four hundred ninety-five psychiatrists (39.6%), 394 male and 101 female, returned their questionnaires in response to one or the other of the two mailings. The mean±SD age of the respondents was 48.3±10.6 years; the mean±SD years of practice since residency was 15.8±10.0. The majority of this sample (35.8%, N=177) indicated that their primary practice setting was private practice, 27.9% (N=138) indicated that they worked in a psychiatric unit of a general hospital, 13.1% (N=65) reported their primary work place as a provincial psychiatric hospital, and 20.2% (N=100) reported working in other settings, including nonpsychiatric medical settings and various ministries associated with the federal and provincial governments. Fifteen respondents (3.0%) did not report their primary practice setting.

Of the respondents, 24.9% (N=123) indicated that they had never filed an Application for Psychiatric Assessment, and 51.1% (N=253) reported filing an average of one or fewer per year. Forty percent (N=198) of the sample reported that they had never filed a Certificate of Involuntary Hospitalization, and 57.6% (N=285) indicated that they file one or fewer per year. Two separate chi-square one-sample tests of independence examining the effects of level of experience and primary practice setting on commitment decisions indicated that respondents' decisions did not differ significantly with respect to their experience and practice settings.

Since each of the 495 returned questionnaires contained three vignettes, all data analyses were based on a sample of 1,485 vignettes; in approximately half of these, the individual met the criteria for commitment, and in the rest he or she did not. The first level of analysis examined the overall rate of recommended hospitalization on both an Application for Psychiatric Assessment and a Certificate of Involuntary Hospitalization. Results indicated that psychiatrists found 47.4% (N=704) of the individuals depicted in the vignettes as hospitalizable on an application and 47.7% (N=708) hospitalizable on a certificate. These figures are remarkably similar; 92.7% of the persons found hospitalizable on an application were also found committable on a certificate, and 92.9% of the individuals found not hospitalizable on an application also were found not hospitalizable on a certificate. A chi-square one-sample test of independence indicated that application decisions did not differ significantly from certificate decisions; thus, all subsequent analyses were performed on application decisions only.

Next, the recommended commitments were examined to determine the vignettes that met the current criteria for commitment and those that did not. While the overall pattern of recommendations for involuntary admission followed appropriate legal standards, some decision errors did occur. Specifically, 25.9% (N=195) of the individuals depicted in the vignettes who clearly met the criteria for commitment were not recommended for involuntary hospitalization, while 19.9% (N=148) of those who did not meet the legal standard were recommended for commitment.

TABLE 1. Factors Involved in 495 Psychiatrists' Decisions About Involuntary Commitment of Patients Described in Hypothetical Vignettes (Analysis of Variance)

Factor	F	df	p	η^2
Main effects	191.81	8	0.001	0.48
Legal standard (LS)	214.12	5	0.001	0.33
Clinical treatability (CT)	17.18	1	0.001	0.01
Alternative resources (AR)	75.28	1	0.001	0.02
Psychotic symptoms (PS)	347.89	1	0.001	0.11
Two-way interactions	8.92	18	0.001	0.05
LS×CT	2.01	5	0.08	<0.00
LS×AR	9.58	5	0.001	<0.00
LS×PS	16.37	5	0.001	0.03
CT×AR	0.11	5	0.74	<0.00
CT×PS	0.28	5	0.60	<0.00
AR×PS	12.18	5	0.001	<0.00
Three-way interactions	6.18	16	0.001	0.03
LS×CT×AR	5.19	5	0.001	<0.00
LS×CT×PS	1.39	5	0.23	<0.00
LS×AR×PS	10.78	5	0.001	0.02
CT×AR×PS	14.78	5	0.001	<0.00

In order to examine what variables (i.e., legal commitability, clinical treatability, alternative resources, psychotic symptoms) contributed to the commitment decisions, a 6×2×2×2 analysis of variance (ANOVA) was performed. Table 1 displays the ANOVA summary. The tests of significance for the ANOVA were supplemented with the eta-squared statistic, which provides an estimate for the amount of variance accounted for by each of the factors and various interactions. From a clinical perspective this latter statistic is more meaningful, since statistical significance, which accounts for little of the explained variance, may be less pragmatically pertinent.

Overall, the legal and nonlegal variables and their respective interactions accounted for approximately 57% of the total variance. As table 1 indicates, all of the main effects were statistically significant and accounted for the largest proportion of this variance (48%). Although there were some significant double and triple interactions, these effects accounted for only 5% and 3% of the variance, respectively. Clearly, the main effects were the most important effects and are the primary focus of this report.

With respect to legal commitability, the responding psychiatrists indicated that they would be more likely to seek involuntary hospitalization of individuals judged to be dangerous to themselves (mean±SD rating=6.29±1.31) than individuals judged to be dangerous to others (5.08±2.05). Individuals judged to be unable to care for themselves would be least likely to be recommended for involuntary hospitalization

(4.37±1.97). As would be expected, individuals depicted in the vignettes as having limited alternative resources would be more likely to be committed (4.47±2.11) than those depicted as having good alternative resources (3.80±2.26), and individuals portrayed as psychotic with little insight would be more likely to be committed (4.88±2.03) than those portrayed as nonpsychotic with good insight (3.37±2.11). Finally, individuals characterized as highly treatable would be more likely to be committed (4.34±2.18) than individuals characterized as not very treatable (3.92±2.22).

Clearly, legal standards—in particular, dangerousness to self and others—and the presence of psychotic symptoms were the most important factors in commitment decisions, while treatability and availability of alternative resources were substantially less influential. Not surprisingly, psychosis and legal commitability accounted for almost the entire interactional variance in the model and revealed an interesting pattern of decision making. Individuals depicted as dangerous to themselves would be committed at about the same rate regardless of their being characterized as psychotic (mean±SD rating=6.50±1.20) or nonpsychotic (6.08±1.39). However, individuals portrayed as dangerous to others would be significantly more likely to be committed if they were depicted as psychotic (6.30±1.17) than if they were depicted as nonpsychotic (3.66±1.92).

DISCUSSION

We believe that several important conclusions concerning decisions about psychiatric civil commitment can be drawn from the results of this study. First, the results suggest that psychiatrists rely primarily upon legal standards and evidence of psychosis in making a decision to commit. Treatability and availability of alternative resources also play a significant but substantively less influential role.

Second, psychiatrists are as likely to commit individuals who are dangerous to themselves as individuals who are dangerous to others. Psychiatrists are likely to commit individuals who are dangerous to themselves regardless of the presence or absence of psychotic symptoms, whereas they are likely to commit those who are dangerous to others only in the presence of psychotic symptoms. These decision-making practices suggest that psychiatrists use involuntary hospitalization to protect both the mentally ill from self-harm and society from the dangerously mentally ill. However, it is important to draw attention to the fact that the psychiatrists in our sample had a higher rate of false negatives (25.9%) (i.e., deciding not to commit when patients met the legal standard for commitment) than of false positives (19.9%) (i.e., deciding to commit when patients did not meet the legal standard). Thus, the psychiatrists' clinical decisions, in effect, served to protect the patients' individual rights and freedoms rather than to protect society from the dangerously mentally ill. This particular finding does not necessarily mean that psychiatrists intentionally protect patients' rights at the expense of protecting society—only that their decision making reflects a tendency toward preserving the rights and freedoms of the individual.

Finally, the fact that in nearly 20% of the returned vignettes, patients who did not meet the established criteria for involuntary hospitalization were, nonetheless, recommended for commitment suggests that in some cases psychiatrists do make decisions to commit when the legal criteria are not met. This result suggests that psychiatrists, although they adhere primarily to legal standards, do in fact consider other factors as sufficient cause to commit. Support for this interpretation comes from other lines of independent research in Canada, where filed commitment certificates have not met legal standards (29), and reports of increasing percentages of commitments despite reform intended to reduce them (4–19, and unpublished 1979 manuscript by V.A. Hiday) in both Canada and the United States. Collectively, these findings suggest that psychiatrists do not rely exclusively on legal criteria.

Given the relatively small amount of variance accounted for by the nonlegal variables manipulated in this study, it is doubtful that psychiatrists as a group rely on availability of resources, clinical treatability, and alternative resources in any systematic fashion. It is more likely that there is a high degree of individual variability in clinical decision making. This individual variation may account for a large segment of the unexplained variance in the overall model. Indeed, the fact that in approximately 26% of the vignettes patients who did meet the established legal criteria were not recommended for commitment, in combination with the finding that about 20% would be committed without meeting the legal criteria, indicates substantial individual variation with respect to decisions not to commit as well as decisions to commit. Perhaps the dangerousness statutes are sufficiently flexible or vague to allow considerable discretion in determining dangerousness (19).

In conclusion, it is important to note that a major limitation of this study is that it relied on hypothetical scenarios, which have unknown relationships with actual commitment decisions. While this particular method allows the reporting of causal influences and interactional effects precluded by field studies, the ecological validity of the results may be compromised. On the one hand, actual commitment decisions most certainly present a wider if not more idiosyncratic range of information, which cannot be captured in a set of vignettes designed to control specific variables. On the other hand, it can be argued that our results represent the best in decision making, in that when responding to the vignettes psychiatrists presumably were not in a time-pressured emergency situation, thus allowing a more thoughtful weighing of facts. For example, hypothetical scenarios clearly do not contain real and potentially problematic consequences for both patients and psychiatrists that are contingent upon final decisions. Similarly, the hypothetical nature of the vignettes may not accurately reflect the actual process of commitment. Many patients committed on an emergency basis, for instance, switch their status to voluntary for a variety of reasons, including change in their clinical status. Such options were not available in our vignettes; the clinical status of the patients remained unchanged. Our finding of a relationship between emergency detention and commitment, therefore, may be of questionable generalizability to actual events and subsequent decisions. Nevertheless, our results have clarified to some extent the causal factors involved in civil commitment decision making that have heretofore not been examined in field studies.

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Somatization: A Spectrum of Severity

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Objective: *The* DSM-III-R *diagnosis of somatization disorder requires that a patient have a specific number of medically unexplained somatic symptoms. This number of symptoms was developed by committee consensus, and it is not clear whether patients with this specific number of symptoms can be differentiated from patients with lower but still substantial numbers of somatic symptoms.* Method: *Fifty-one percent of 767 high utilizers of two primary care clinics were identified as distressed by an elevated SCL anxiety, depression, or somatization scale score or by their primary care physician. The Diagnostic Interview Schedule (DIS) was completed on 119 distressed high utilizers who were randomly assigned to an intervention group in a controlled trial of psychiatric consultation. The 119 distressed high utilizers were separated into four categories according to the number of unexplained somatic symptoms found on the DIS and were compared on demographic, psychiatric distress, disability, medical, and health utilization variables.* Results: *The data suggest that many clinical and behavioral features of somatization are significantly more common in patients with four to 12 medically unexplained somatic symptoms rather than changing dramatically at the diagnostic threshold for somatization disorder. The data also showed that patients who meet the* DSM-III-R *criteria for somatization disorder are severely ill and have a high burden of psychiatric illness and disability.* Conclusions: *The results suggest that the* DSM-IV *somatoform disorders section should include somatization disorder, an abridged definition of somatization disorder often associated with anxiety and depression, as well as a type of somatization associated with an adjustment disorder.*

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The diagnosis of somatization has evolved significantly since the term "neurasthenia" was first used in 1868 to describe patients with an aggregate of physical and psychological symptoms (1). Perley and Guze (2) described 59 symptoms in 10 categories as characteristic of Briquet's syndrome and required the presence of at least 25 medically unexplained symptoms in nine categories for the diagnosis. The number of symptoms was later found to be highly correlated with the number of symptom categories, so *DSM-III* dropped the requirements about the distribution of symptoms in categories and required women to have 14 and men 12 of 37 characteristic symptoms. *DSM-III-R* altered these requirements slightly so that men and women both had to have 13 medically unexplained symptoms to meet the criteria.

Several studies (3, 4) suggested that patients with somatization disorder are relatively rare in community and primary care populations and are far outnumbered by persons with fewer medically unexplained somatic symptoms. Somatization in primary care and in the community is frequently accompanied by symptoms of depression and anxiety (4–8). Escobar et al. (4, 5) defined a less severe form of somatization occurring in approximately 4% of the general population. This abridged definition of somatization required four medically unexplained symptoms in a man and six in a woman on the 37-item somatization disorder section of the National Institute of Mental Health Diagnostic Interview Schedule (DIS). This abridged definition of somatization was found to correlate with medical utilization, disability, and lifetime diagnoses of dysthymic disorder and major depression (4, 5). Swartz et al. (6) also defined a subsyndromal form of somatization that was associated with higher rates of seeking health care,

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but at an intermediate level between the general population and patients with somatization disorder. Approximately 11.6% of the general population met the criteria for this category. Several other primary care and community studies (3, 4, 7) have described a large subgroup of people who have multiple, unexplained somatic symptoms but fall short of meeting the criteria for somatization disorder.

One controversy stimulated by these data is whether somatization should be based on a dichotomous framework or whether it represents a spectrum, with somatization disorder at one extreme. If somatization is a continuum, one would hypothesize that as the number of medically unexplained somatic symptoms increases, so would the rates of coexisting psychiatric disorders, disability, and health care use. The aim of the present report is to compare differences in demographic variables, medical utilization, *DSM-III-R* diagnoses, and disability indices in a sample of patients with high utilization of primary care and with increasing levels of somatization.

METHOD

Subjects

The setting for this study was two primary care clinics of Group Health Cooperative of Puget Sound, a health maintenance organization with 23 primary care clinics serving over 300,000 persons in Washington State. The target population included patients between the ages of 18 and 75 whose utilization in the prior 12 months placed them in the top 10% of the number of ambulatory health care visits for their age and sex groups.

The method used to select patients who were high utilizers of primary care for a randomized trial of psychiatric consultation-liaison has been described elsewhere (8). In brief, 767 high users of primary care were screened with the SCL-90-R anxiety, depression, and somatization scales (9). Patients who scored one standard deviation or more above the mean, based on published SCL norms and SCL data from Group Health Cooperative, or who were identified as distressed by their physician became eligible for the intervention phase of the study. Overall, 392 (51.1%) of 767 patients met one or more of the three screening criteria and were eligible for a baseline interview followed by randomization to the intervention or control group. Fifty-three subjects with a positive screening result were excluded from eligibility for the baseline interview and randomization because sample size requirements for the controlled trial had been satisfied.

Among the 339 subjects eligible for randomization, 251 (74.0%) accepted randomization and completed the baseline interview. Subjects accepting randomization did not differ from those declining to participate in age, sex, or SCL somatization score, but there was a trend toward patients declining randomization to have a lower mean score on SCL anxiety and depression items (0.72 among persons declining versus 0.87 among persons accepting; $\chi^2=1.93$, df=339, p=0.05). Among the 251 subjects who were randomized, 124 were assigned to the psychiatric intervention and 127 were assigned to the control group. A total of 119 (96.0%) of the 124 patients assigned to intervention completed the in-clinic examination procedure.

Procedure

During the psychiatric liaison examination, each patient received a 1-hour interview in which the DIS, Version 3A (10), was administered by one of the two study psychiatrists (W.K. or P.L.). The DIS sections on somatization disorder, panic disorder generalized anxiety disorder, phobias, major depression, dysthymic disorder, and alcohol abuse/dependence were administered. Both psychiatrists were highly experienced in administering the DIS to medical patients. Minor changes were made in the panic and generalized anxiety disorder sections in accordance with *DSM-III-R* criteria. The DIS was also modified to inquire about current symptoms of major depression (11). Psychiatric diagnoses were made according to *DSM-III-R* criteria for a current mental disorder if symptoms had been present in the prior month. We also report lifetime diagnoses. After the DIS was completed, each patient received a half-hour interview conducted by the psychiatrist with the primary care physician present. In this intervention the psychiatrist reviewed the salient points in the patient's clinical psychiatric status and social and developmental history. The psychiatrist and primary care physician then negotiated a mutually acceptable treatment plan with the patient Patients also completed several questionnaires that included items on chronic medical illness, functional disability (12), and the tendency to amplify physiologic sensations (13).

The primary care physicians completed a Physician Review Form for each study patient (N=251) before the psychiatric intervention and 6 months after randomization. The form included physician ratings of severity of physical illness, severity of psychiatric illness, and the patient's tendency to amplify physical symptoms. Each of these factors was rated on a Likert scale (rating=1–5).

The 119 distressed high utilizers of primary care who were assigned to the psychiatric intervention and completed the in-clinic examination procedure were separated into four categories according to the number of medically unexplained somatic symptoms found on the 37-item somatization disorder section of the DIS. Group 1 consisted of women with fewer than six and men with fewer than four somatic symptoms, group 2 consisted of women with 6–8 and men with 4–8 somatic symptoms, group 3 consisted of women and men

TABLE 1. Demographic Characteristics of Four Groups of Distressed High Users of Primary Care Who Had Somatization Disorder Symptoms

Group	Age (years)[a]		Percent Women[b]	Percent White[c]	Education (years)[d]		Percent With Income Less Than $25,000[e]	Percent Working Full-Time[f]	Percent Married[g]
	Mean	SD			Mean	SD			
Group 1: women with fewer than 6 and men with fewer than 4 somatic symptoms (N=31)	43.9	14.16	51.6	71.0	14.97	2.74	53.6	64.5	51.6
Group 2: women with 6–8 and men with 4–8 somatic symptoms (N=40)	42.2	9.50	40.0	77.5	15.07	2.57	28.9	82.5	45.0
Group 3: women and men with 9–12 somatic symptoms (N=21)	46.8	14.73	85.7	90.5	15.05	2.75	52.4	38.1	28.6
Group 4: women and men with 13 or more somatic symptoms (N=27)	47.9	10.75	88.9	73.1	14.08	2.31	54.5	44.4	51.8

[a] $F=1.36$, df=3, 115, n.s.

[b] $\chi^2=22.98$, df=3, $p<0.001$.

[c] $\chi^2=3.03$, df=3, n.s.

[d] $F=0.93$, df=3, 115, n.s.

[e] $\chi^2=6.06$, df=3, n.s.

[f] $\chi^2=15.72$, df=3, $p<0.001$.

[g] $\chi^2=3.34$, df=3, n.s.

with 9–12 somatic symptoms, and group 4 consisted of women and men with 13 or more somatic symptoms. These cutoffs were chosen to be consistent with the abridged definition of somatization (5) and to analyze a subgroup with a symptom cutoff between somatization disorder and this abridged definition.

Statistical Analyses

Analyses of variance (ANOVAs) using the general linear model procedure of SPSS (14) was employed to examine group differences in the continuous demographic and *DSM-III-R* symptoms. Gender was used as a covariate in these analyses. In all cases it proved to be nonsignificant, and the analyses were recalculated without gender. Tukey's Studentized Range Test (Honestly Significant Difference) was used for post hoc tests of group differences. The dichotomous demographic and *DSM-III-R* diagnoses were analyzed with chi-square analyses.

We examined sets of indicators representing the patients' self-reported psychological and physical symptoms (five indicators), disability (four indicators), health care utilization (three indicators), and physicians' assessments (four indicators). These sets of indicators were subjected to multivariate analyses of variance (MANOVAs). Due to the number of indicators and their intercorrelations, MANOVAs were used to control the experiment-wise type I error rate. Each MANOVA provided a global test of differences in indicators among the four somatization groups. In addition, this global test was partitioned into three orthogonal polynomial tests for linear, quadratic, and cubic trends in the group means. The importance of partitioning group differences into trends within the data was to give evidence about the pattern of group differences. A significant group main effect does not tell much about the pattern of group means; however, a significant linear trend in the absence of significant quadratic and cubic trends tells us that the mean of the indicators increases with increasing severity of somatization groups.

In all four MANOVAs gender was initially used as a covariate. However, since gender was always nonsignificant, the analyses were recalculated without controlling for gender. Although there were no main effects of gender on any other outcome variables, we cannot be sure that there were no interactions of gender with somatization groups. We were unable to calculate these interactions because groups 3 and 4 each contained only three men, thus precluding a two-way factorial design.

Univariate ANOVAs were used to examine which indicators contributed to the global test significance. When results of univariate tests were significant, post hoc analyses using Tukey's Studentized Range Test were conducted to further control for the type I experiment-wise error rate.

RESULTS

Demographic Characteristics

There were no significant differences in age, race, education, income, or marital status (table 1). The groups did differ in gender and employment status. Although there were significantly more women in

TABLE 2. ***DSM-III-R*** **Diagnoses of Four Groups of Distressed High Users of Primary Care Who Had Somatization Disorder Symptoms**

Group[a]	Total Current Diagnoses[b]		Total Lifetime Diagnoses[c]		Lifetime Depressive Symptoms[d]		Lifetime Panic Disorder[e]		Lifetime Major Depression[f]		Lifetime Dysthymic Disorder[g]	
	Mean	SD	Mean	SD	Mean	SD	N	%	N	%	N	%
Group 1 (N=31)	0.55	0.85	1.23	1.28	3.81	2.44	1	3.2	14	45.2	7	22.6
Group 2 (N=40)	0.68	0.94	1.93	1.12	5.32	1.89	8	20.0	30	75.0	9	22.5
Group 3 (N=21)	0.57	0.81	1.71	1.27	5.10	2.05	4	19.0	15	71.4	5	23.8
Group 4 (N=27)	1.41	1.62	2.63	1.55	6.10	1.98	13	48.1	22	81.5	17	63.0

[a] See table 1 for description of groups.
[b] F=3.78, df=3, 115, $p<0.01$; group 4 significantly different from group 1.
[c] F=5.78, df=3, 115, $p<0.001$; group 4 significantly different from group 1.
[d] F=6.04, df=3, 115, $p<0.001$; groups 2, 3, and 4 significantly different from group 1.
[e] χ^2=17.78, df=3, $p<0.001$; groups 2, 3, and 4 significantly different from group 1.
[f] χ^2=10.71, df=3, $p<0.001$; groups 2, 3, and 4 significantly different from group 1.
[g] χ^2=15.48, df=3, $p<0.001$; group 4 significantly different from group 1.

TABLE 3. Self-Reported Physical and Psychological Symptoms of Four Groups of Distressed High Users of Primary Care Who Had Somatization Disorder Symptoms[a]

Group[b]	Self-Reported Physical Symptoms[c]		SCL Anxiety/ Depression Score[d]		SCL Somatization Score[e]		Barsky Amplification[f]		Self-Reported Chronic Diseases[g]	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Group 1 (N=31)	4.06	2.38	0.71	1.03	0.33	0.89	1.19	0.59	0.97	0.91
Group 2 (N=40)	4.38	1.79	1.03	1.14	0.47	0.83	1.36	0.66	1.00	1.09
Group 3 (N=21)	5.67	2.35	0.92	1.68	1.05	1.62	1.67	0.64	1.33	1.46
Group 4 (N=27)	7.81	2.82	1.32	1.90	2.12	1.73	1.72	0.60	1.96	1.48

[a] The F statistic represents a partitional univariate test for linear trend; df=1, 114.
[b] See table 1 for description of groups.
[c] F=41.99, df=1, 144, $p<0.001$; groups 3 and 4 significantly different from group 1.
[d] Adjusted for age and sex; F=2.71, n.s.
[e] F=31.53, $p<0.001$; groups 3 and 4 significantly different from group 1.
[f] F=13.13, $p<0.001$; groups 3 and 4 significantly different from group 1.
[g] F=10.47, $p<0.01$; group 4 significantly different from group 1.

groups 3 and 4 than in groups 1 and 2, gender was not a significant covariate in any of the statistical analyses. In addition, the results were recalculated for women alone. The only result that changed was employment status. When men were excluded, the group differences in employment status were nonsignificant.

Diagnoses and Symptoms

The total number of current and lifetime *DSM-III* diagnoses (major depression, dysthymic disorder, generalized anxiety disorder, panic disorder, and alcohol abuse/dependence) differed significantly among the four groups (table 2). In both cases, group 4, which met *DSM-III* criteria for somatization disorder, had significantly more current and lifetime diagnoses than the other three groups. The number of *DSM-III* lifetime depressive symptoms also differed among the groups. Group 1 had significantly fewer symptoms than the other three somatization groups, which did not differ significantly in the number of depressive symptoms. The four groups had significantly different rates of lifetime panic disorder, lifetime major depression, and lifetime dysthymic disorder. The somatization disorder group (group 4) had significantly higher rates of lifetime panic disorder and lifetime dysthymic disorder than the other three groups. Group 1 had significantly lower rates of lifetime panic disorder and lifetime major depression than the other three groups.

The five indicators (table 3), taken as a set, differed significantly among the four groups (F=3.78, df=15, 304, $p<0.001$). In addition, these indicators had a significant linear trend (F=11.43, df=5, 110, p=0.001) and nonsignificant quadratic and cubic trends. Univariate tests revealed a significant linear trend in group differences in all but one indicator (SCL anxiety/depression scale). As expected, the number of self-reported physical symptoms and SCL somatization scale scores increased significantly with severity of somatization. Group 4 reported significantly more symptoms than the other three groups. Group 3 also differed significantly from group 1. There was a significant linear trend in amplification of symptoms with increasing levels of somatization, with group 1 reporting significantly less amplification of symptoms than groups 3 and 4. There was a significant linear trend in the number of patient-reported chronic diseases, with the somatization disorder group reporting more diseases than groups 1 and 2.

TABLE 4. Self-Reported Disability and Health Care Utilization of Four Groups of Distressed High Users of Primary Care Who Had Somatization Disorder Symptoms[a]

	Bed Days in Prior Year[c]		Days With Decreased Activities in Prior Year[d]		Two or More Activities of Daily Living Impaired[e]		Health Rated as Fair/Poor[f]		Total Visits in 1 Year[g]		Phone Calls per Month[h]		Requests for Referrals[i]	
Group[b]	Mean	SD	Mean	SD	N	%	N	%	Mean	SD	Mean	SD	Mean	SD
Group 1 (N=31)	6.23	9.28	44.97	91.03	12	38.7	13	41.9	13.32	7.70	0.84	1.39	0.61	0.76
Group 2 (N=40)	13.25	17.39	32.32	42.58	16	40.0	15	37.5	13.90	7.50	0.85	0.86	0.60	0.93
Group 3 (N=21)	20.47	32.02	79.70	118.90	9	42.9	11	52.4	16.10	10.53	1.62	1.91	0.90	2.16
Group 4 (N=27)	26.18	41.24	130.68	147.71	16	59.3	19	70.4	19.41	9.88	2.11	1.93	1.41	3.84

[a] The F statistic represents a partitional univariate test for linear trend; df=1, 115.
[b] See table 1 for description of groups.
[c] $F=8.07$, $p<0.01$; group 4 significantly different from group 1.
[d] $F=12.22$, $p<0.001$; group 4 significantly different from group 1.
[e] $F=5.55$, $p<0.05$; group 4 significantly different from group 1.
[f] $F=4.38$, $p<0.05$; group 4 significantly different from group 1.
[g] $F=7.92$, $p<0.01$; group 4 significantly different from group 1.
[h] $F=13.52$, $p<0.001$; group 4 significantly different from group 1.
[i] $F=2.24$, df=1, 115, n.s.

Disability and Health Care Utilization

Results of the global test for group differences in patient disability indicators (table 4) were significant ($F=2.23$, df=12, 280, $p<0.01$). Group means on the disability indicators increased in a significant linear trend as the number of somatic symptoms in the groups increased ($F=4.30$, df=4, 106, $p<0.003$). Results of the quadratic and cubic tests were nonsignificant. All four disability indicators (number of days in bed, number of days with decreased activities in the last year, number of activities of daily living impaired, and self-reported ratings of health [from fair to poor]) increased significantly and linearly with increasing numbers of unexplained somatic symptoms. The somatization disorder group (group 4) was significantly more disabled than group 1 on all measures of disability and significantly more disabled than group 2 on number of days with decreased activities and ratings of health.

The groups differed globally on the measures of health care utilization ($F=2.32$, df=9, 275, $p<0.02$) (table 4), and once again a significant linear trend fit the data ($F=6.46$, df=3, 113, $p<0.001$), while the quadratic and cubic trends did not. The global differences were due to group differences in the number of total visits to the clinic in the year before screening and number of phone calls to the clinic. The groups did not differ in the number of requests for referrals. Although there was a significant linear trend in the number of total visits and phone calls across the groups, post hoc tests revealed that these results were due to differences between the somatization disorder group and groups 1 and 2. However, utilization differences may have been attenuated because patients were selected on the basis of high medical utilization levels.

Physicians' Assessments

In general, the physicians' assessments (table 5) differed among the four groups ($F=2.75$, df=12, 251, $p<0.002$). A global linear trend was found to best fit the pattern of the means ($F=6.21$, df=4, 95, $p<0.001$), while the quadratic and cubic trends were nonsignificant. The physicians did not perceive significant differences in the severity of the physical health problems in these groups. However, they did perceive that the groups differed in the severity of psychiatric illness, patients' tendency to amplify their symptoms, and the frustration of caring for these patients. Post hoc tests revealed that group 1 was viewed as significantly less psychiatrically ill, less likely to amplify symptoms, and less frustrating to care for than the other three groups. The other three somatization groups did not differ among themselves.

DISCUSSION

Our data suggest that many clinical and behavioral features associated with somatization were significantly more common in patients in groups 2 and 3 (men with four to 12 and women with six to 12 medically unexplained symptoms) rather than changing dramatically at the diagnostic threshold (13 symptoms) for somatization disorder. Patients in groups 2, 3, and 4 had significantly higher rates of lifetime panic disorder and major depression. Moreover, self-re-

TABLE 5. Physician Review Form Ratings of Four Groups of Distressed High Users of Primary Care Who Had Somatization Disorder Symptoms[a]

Group[b]	Diagnosis of Moderate to Severe Medical Problems[c]		Diagnosis of Moderate to Severe Mental Health Problems[d]		Patient Amplifies Symptoms[e]		Patient Is Frustrating[f]	
	N	%	N	%	N	%	N	%
Group 1 (N=31)	16	51.6	13	41.9	8	25.8	4	12.9
Group 2 (N=40)	21	52.5	35	87.5	22	55.0	17	42.5
Group 3 (N=21)	7	33.3	16	76.2	15	71.4	10	47.6
Group 4 (N=27)	20	74.7	22	81.5	19	70.4	9	33.3

[a] The F statistic represents a partitional univariate test for linear trend; df=1, 115.
[b] See table 1 for description of groups.
[c] F=1.04, n.s.
[d] F=21.74, p<0.001; groups 2, 3, and 4 significantly different from group 1.
[e] F=11.06, p<0.001; groups 2, 3, and 4 significantly different from group 1.
[f] F=4.59, p<0.05; groups 2, 3, and 4 significantly different from group 1.

ported physical symptoms, amplification of physical symptoms, self-reported disability, and medical utilization increased linearly with number of somatic symptoms. Primary care physicians agreed with the DIS assessment of patients who somatized (groups 2, 3, and 4) as having worse mental health and amplifying physical symptoms, as well as being significantly more frustrating patients than patients with low levels of somatization.

Our data suggest the potential utility of viewing somatization as a continuum on which increasing levels of somatic symptoms are indicative of increasing distress, disability, and maladaptive illness behavior. Rather than a discrete cutoff point for somatization, such as *DSM-III-R*'s requirement of 13 unexplained somatic symptoms for the diagnosis of somatization disorder, our data suggest that patients with nine to 12 symptoms may be almost as severely disabled as those with 13. These data provide support for the inclusion in *DSM-IV* of one or more categories of less severe types of somatization. Our data also support the continued use of *DSM-III-R* criteria for somatization disorder. Patients with *DSM-III-R* somatization disorder were severely ill and had a high burden of psychiatric illness and disability on virtually every factor measured.

Although the data presented are limited to distressed high users of primary care, there are extensive data suggesting that somatization can occur in normal individuals and in groups under great social stress and can become enmeshed with difficulties in social functioning in the family and the workplace (15, 16). The *DSM-IV* somatoform disorders section could include somatization disorder, an abridged definition of somatization often associated with anxiety and depressive disorders, as well as a type of somatization associated with adjustment to stress and somatic idioms of distress that occur in patients without psychiatric illness. This division of somatization would make *DSM-IV* more applicable to the clinical realities in primary care medicine, where somatization associated with social stress, anxiety, depression, and functional disability is much more common than somatization disorder (3, 4, 6, 16, 17).

Another ramification of our data is that patients with somatization are more likely to suffer from anxiety and depressive disorders than has been previously recognized. The primary care physicians considered the severity of anxiety and depressive disorders as essentially similar in all three groups of patients with multiple unexplained somatic symptoms, and DIS lifetime panic and major depressive disorders were also significantly more prevalent in the three somatization groups than in group 1. This connection between anxiety, depression, and somatization is supported by multiple studies which have found that somatization and high utilization of health care are frequently associated with major depression and panic disorder (4, 17, 18). Moreover, studies of the treatment of panic disorder and major depression (19, 20) have found that improvement in anxiety and depression is associated with decreased hypochondriacal concern and reporting of physical symptoms. Although the definitions of panic disorder and major depression have been narrowed to the key autonomic and vegetative symptoms, as well as cognitive and emotional symptoms, there is now abundant evidence that a wide range of physical symptoms accompany anxiety and depressive illness (4, 17–21).

There are several mechanisms that may explain the association between mental illness and medically unexplained somatic symptoms. First, both psychological and somatic symptoms may result from the same underlying physiological abnormalities. Thus, neurophysiologic dysfunction and the resulting autonomic nervous system dysregulation may cause panic disorder and affective illness as well as somatic symptoms such as irritable bowel syndrome, headaches, hyperacidity and epigastric distress, labile hypertension, and mitral valve prolapse. Such dysfunction may also contribute to worsening symptoms of a concurrent chronic medical disease such as angina pectoris (22, 23).

It is also possible that depression and anxiety lower the threshold at which minor symptoms are perceived. These disorders may increase perception of or amplify bodily complaints. Experimental work suggests that depressive mood fosters illness-related memories and a negative view of one's health (24).

Chronic physical symptoms, whether psychological or somatic in origin, may also play a role in initiating or provoking depression and anxiety through behavioral mechanisms. For instance, many patients with chronic pain describe their pain as decreasing their enjoyment of formerly pleasurable activities, contributing to progressive withdrawal from social activities, and leading to despair that nothing can be done to relieve the pain. These decrements in activity levels and social reinforcement and feelings of hopelessness and helplessness may contribute to or initiate depressive illness (25). At the same time, chronic physical symptoms may contribute to anxiety and depression by causing dysregulation of sleep and autonomic nervous system function, which then may lead to the maladaptive cognitive and behavioral changes associated with anxiety and depression (25, 26).

Our clinical data cannot shed much light on these alternative, perhaps mutually reinforcing, mechanisms linking somatization, psychological disorders, and functional disability. Our data do suggest that somatization can be productively viewed as a continuum of illness, as well as a discrete disorder. Our data also support previous research indicating that significant functional difficulty, interpersonal difficulties, and psychological impairment are associated with somatization even among persons not meeting full *DSM-III-R* criteria for somatization disorder. These data suggest that a modification of the *DSM-III-R* somatoform disorder section is warranted. Most patients with diffuse unexplained somatic symptoms evaluated in primary care settings and in community samples have a treatable psychiatric disorder (anxiety or depression) or are responding to stressful life events (3, 4, 6, 15–18). Failure to distinguish somatization as part of an adjustment disorder from somatization due to anxiety and depression, or from somatization as a serious, chronic psychiatric disorder (somatization disorder), makes psychiatric classification of somatoform disorders less applicable to the patient problems that are seen in primary care medicine.

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Glucocorticoid Level and Neuropsychiatric Symptoms in Homosexual Men With HIV Infection

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Objective: There is a controversial literature suggesting that stress, anxiety, and depression are harmful to the immune system and therefore to health. Preclinical studies indicate that activation of the hypothalamic-pituitary-adrenal (HPA) axis by stress may be responsible for immunocompromise. The goal of this study was to assess this phenomenon in human immunodeficiency virus (HIV) infection. Method: Homosexual men in the community who did not meet modified Centers for Disease Control criteria for acquired immune deficiency syndrome (AIDS) were recruited for the study; 113 of the men were HIV positive and 77 were HIV negative. Very few of the men studied suffered from depression or anxiety disorder at the time of the first assessment. Twenty-four-hour urinary free cortisol levels were obtained from the 112 HIV-positive and 75 HIV-negative men whose 24-hour urine volumes were 500 ml or more. Cortisol levels were correlated with measures of medical, immunological, neurological, and psychiatric status. Results: Small but significant correlations between 24-hour urinary free cortisol and medical status, level of depression, and level of anxiety were found in the HIV-positive group. There was no relationship between cortisol level and the number of CD4+ or CD8+ T lymphocytes or the CD4-CD8 ratio. Conclusions: Although HPA activation may be associated with stress in cases of HIV infection, it does not seem to be associated with further loss of CD4+ T lymphocytes. Subjects with HIV infection with the most evidence of medical complications may also be the most anxious and depressed.

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The mechanism by which psychological morbidity may affect the immune system is not known (1–5). In the preclinical literature, it has been suggested that activation of the hypothalamic-pituitary-adrenal (HPA) axis by stress may produce immunocompromise (6, 7). Not all studies support this, however (8). Glucocorticoids have profound and varied effects on human immune function, but many of these are in the direction of diminishing immunocompetence (9). It is well established that at least a subgroup of patients with affective disorder have higher cortisol production (10); some studies also suggest that this occurs in humans experiencing stress or suffering from anxiety disorder (11).

Human immunodeficiency virus (HIV) infection typically manifests a long latency before clinical manifestations of the acquired immune deficiency syndrome (AIDS) (12, 13). Many "co-factors" have been suggested as possible activators of HIV, including stress, depression, and anxiety disorder. There is in vitro evidence that glucocorticoids enhance replication of HIV (14). Of the many immunological effects demonstrated for glucocorticoids, depression of T lymphocyte number, percent, and function is important (9) because HIV has special tropism for the class of T lymphocytes bearing the CD4 receptor. The hallmark of HIV infection is the progressive loss of CD4+ T lymphocytes—also known as "helper lymphocytes"—leading to collapse of the entire immune system. Thus, stress-induced HPA activation might be an important "co-factor" of HIV disease progression.

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As part of an ongoing, longitudinal study of subjects with HIV infection, we considered the possibility that infected subjects who were also highly anxious or depressed might have elevated cortisol levels, indicating HPA activation, and concomitantly depressed immune function. This could result in more rapid development of medical signs and symptoms of HIV infection. We collected 24-hour urine samples for measurement of urinary free cortisol level as an index of HPA activation, along with measures of immune function, medical status, neurological status, neuropsychological test performance, and psychiatric status. We hypothesized that if stress leads to decline in medical or neurological status among subjects infected with HIV through the mechanism of glucocorticoid-induced immunosuppression, then patients with the most evidence of anxiety and depression should have the highest levels of 24-hour urinary free cortisol, the fewest CD4+ T lymphocytes, and the most HIV-related medical signs and symptoms. Our results should be considered preliminary because at the time of this first assessment, as described later in this paper, very few of our subjects actually suffered from serious clinical depression or anxiety disorder.

METHOD

The subjects in this report are participants in a longitudinal study of the behavioral and nervous system effects of HIV infection. At baseline the male homosexual study group consisted of 124 HIV-positive and 84 HIV-negative subjects. All of the men were asked to participate in the cortisol portion of the study, and most of them complied.

Cortisol data were collected from 113 homosexual men who tested positive and 77 homosexual men who tested negative for HIV infection by enzyme-linked immunosorbent assay (ELISA) and Western Blot. We required that subjects already know their HIV status for at least 1 month before admission to the study. HIV-positive subjects were excluded if they met Centers for Disease Control (CDC) criteria for AIDS. This ensured that the HIV-positive subjects were at relatively early stages of disease progression. Table 1 shows the age, education level, Hollingshead socioeconomic status (15), and race of 112 of the men with and 75 of the men without HIV infection. These subjects were recruited for a longitudinal study involving medical, psychiatric, psychosocial, psychosexual, neurological, and neuropsychological assessment every 6 months for 5 years.

Subjects were asked to begin collecting all urine the evening before reporting to our facility for the first of these 6-month assessments. Urine collection was then continued throughout the next day while the subject was undergoing the battery of assessments described later in this paper. Thus, for a large part of the 24-hour period of urine collection the subject was in the clinic and could be reminded to save all urine.

TABLE 1. Demographic Characteristics of 187 Homosexual Men With or Without HIV Infection

Characteristic	Men With HIV Infection (N=112)	Men Without HIV Infection (N=75)
Age (years)		
Mean	38.3	37.4
SD	7.9	8.8
Education (grade)[a]		
Mean	15.9	16.5
SD	2.6	2.0
Socioeconomic status[b]		
Mean	48.5	53.0
SD	12.6	9.4
Race (number of subjects)		
White	96	64
Hispanic	7	6
Black	4	2
Black or Hispanic	1	0
Asian or Pacific Islander	2	2
Refused to provide information	2	1

[a] $t=1.83$, df=179, $p<0.07$.
[b] $t=2.79$, df=184, $p<0.006$.

At the end of the 24-hour period, the total volume of urine was measured and then a 25-cc aliquot was frozen for cortisol analysis. Urinary free cortisol was measured in our behavioral endocrinology laboratory by using a double antibody direct radioimmunoassay procedure. The coefficients of variance for intra- and interassay were 2.1% and 3.1%, respectively.

During the course of the assessment day the subjects also underwent the following tests and interviews.

1. A medical history was taken by a research nurse, and a physical examination was then performed by a physician blind to the subject's HIV test results. Medical signs and symptoms were summarized for each subject in two ways. First, HIV-positive subjects were assigned a score on a medical staging system devised by our group. This four-tier system is shown in appendix 1. Within each tier the examining physician assigned a number based on his or her subjective judgment of medical severity. By design, no subject with a score greater than 29 was admitted to the study. Second, a 20-item symptom checklist was created. Shown in appendix 2, the symptom checklist includes signs and symptoms of HIV infection. All subjects were assigned a score based on the number of signs or symptoms for which they were positive. Unlike the medical staging system, each sign or symptom in the symptom checklist carries an equal weight.

2. The subjects participated in a psychiatric interview using the Structured Clinical Interview for DSM-III-R (SCID) (16). Included in this part of the assessment was the Hamilton Rating Scale for Depression, the Hamilton Rating Scale for Anxiety, and a global assessment of functioning scale. The global assessment of functioning scale enables a clinician to indicate his

TABLE 2. Medical, Immunological, and Neurological Characteristics of 187 Homosexual Men With or Without HIV Infection

Characteristic	Men With HIV Infection (N=112)		Men Without HIV Infection (N=75)			
	Mean	SD	Mean	SD	t	p
CD4+ cells/μl	401.8	226.4	828.2	274.9	11.55	0.001
CD8+ cells/μl	834.9	446.0	538.1	213.1	6.06	0.001
CD4-CD8 ratio	0.6	0.4	1.7	0.6	14.02	0.001
Hamilton depression scale score	4.4	4.1	3.3	3.6	1.95	0.052
Hamilton anxiety scale score[a]	4.0	3.8	3.0	3.7	1.58	n.s.
Global assessment of functioning scale score	68.6	8.1	69.2	8.9	0.43	n.s.
20-item symptom checklist score	2.2	1.5	0.9	1.0	7.26	0.001
Medical stage	12.3	8.9	—	—	—	—
Global performance rating	1.2	1.1	1.2	1.2	0.21	n.s.
Neuropsychological impression	0.5	0.7	0.5	0.7	0.55	n.s.
Kurtzke Disability Status Scale for Multiple Sclerosis score	1.2	0.7	1.2	0.6	0.28	n.s.

[a] N=99 for the men with HIV infection; N=74 for the men without HIV infection.

or her overall judgment of a person's psychological, social, and occupational functioning on a scale that assesses mental health or illness. Ratings range from 1 to 90; scores of 70 and above generally indicate positive mental health, and scores below 40 are usually found among hospitalized psychiatric patients.

3. A neurological examination was conducted by a neurologist blind to HIV status. The results of the examination were summarized by using a modification of the Kurtzke Disability Status Scale for Multiple Sclerosis (17), which rates as normal or abnormal nine categories of neurological function.

4. An extensive neuropsychological test battery assessing all domains of neuropsychological functioning was conducted by trained neuropsychological technicians blind to HIV status. The results of this battery were summarized in two ways. First, a global performance rating was devised to summarize overall neuropsychological performance with reference to normative data and to rank performance along a continuum of severity. The global performance rating has anchor points: 0=no performance deficit, 1=borderline performance in two or more areas, 2=defective performance in one area, 3=defective in two or more areas, and 4=defective in memory and in two or more other areas. Second, the neuropsychological technician assigned a score—the neuropsychological impression—based on the independent judgment of two neuropsychologists that represents a clinical impression of normal, borderline, or abnormal performance. Interrater reliability and test-retest reliability for the Kurtzke, global performance rating, and neuropsychological impression scales as assessed by our group have been discussed elsewhere (18, 19).

5. Blood samples were drawn for measurement of the number and percent of CD4+ T lymphocytes, CD8+ T lymphocytes, and the ratio of CD4+ to CD8+ T lymphocytes.

Blood was also drawn for confirmatory HIV testing by ELISA and Western Blot, and all subjects were given pre- and post-HIV-test counseling, even though they already knew their serostatus. Informed written consent was obtained from each subject.

The mean 24-hour urinary free cortisol levels of HIV-positive and -negative groups were compared by t test. Within each of the two groups, we used Pearson product-moment correlations to examine the relationship between urinary free cortisol level and 11 variables. All significance levels are two-tailed, and the alpha level was set at 0.05.

RESULTS

Before data analysis, we dropped 24-hour urinary free cortisol data for three subjects because their total urine volume was less than 500 ml. The remainder of the subjects provided urine volume consistent with a 24-hour collection. This left 112 in the HIV-positive group and 75 in the HIV-negative group.

There were no statistically significant differences between HIV-positive and -negative groups for age, years of education, or race (see table 1). Although the difference in socioeconomic status between the two groups was statistically significant, inspection of table 1 indicates that the actual difference was very small and not meaningful.

For the HIV-positive subjects, the mean medical stage score was 12.3 and the mean±SD number of CD4+ T lymphocytes was 402±226/μl. This indicates a group with relatively few medical symptoms and relatively intact immunological status.

Table 2 shows means for the two groups on medical, immunological, psychiatric, and neurological measures. As expected, HIV-positive subjects had fewer CD4+ T lymphocytes, more CD8+ T lymphocytes, lower CD4-CD8 ratios, and more symptoms on the symptom checklist than HIV-negative subjects. HIV-positive subjects also had significantly higher mean Hamilton depression scale scores, but their mean of 4.4±4.1 indicates a group with minimal depression.

TABLE 3. Pearson Correlations Between 24-Hour Urinary Free Cortisol and Other Variables for 187 Homosexual Men With or Without HIV Infection

	Correlation With 24-Hour Urinary Free Cortisol			
	Men With HIV Infection (N=112)		Men Without HIV Infection (N=75)	
Variable	r (df=110)	p	r (df=73)	p
20-Item symptom checklist score	0.19	0.04	−0.02	n.s.
Medical stage	0.20	0.04	—	—
Hamilton depression scale score	0.25	0.01	0.08	n.s.
Hamilton anxiety scale score[a]	0.23[b]	0.03	0.13[c]	n.s.
Global assessment of functioning scale score	−0.02	n.s.	0.01	n.s.
Kurtzke Disability Status Scale for Multiple Sclerosis score	0.10	n.s.	−0.04	n.s.
Global performance rating	−0.04	n.s.	−0.02	n.s.
Neuropsychological impression	0.07	n.s.	−0.09	n.s.
CD4+ cells	0.01	n.s.	−0.14	n.s.
CD8+ cells	0.10	n.s.	−0.07	n.s.
CD4-CD8 ratio	0.02	n.s.	−0.11	n.s.

[a] N=99 for the men with HIV infection; N=74 for the men without HIV infection.
[b] df=97.
[c] df=72.

There were no significant differences between groups in Hamilton scale scores, global assessment of functioning scale score, global performance ratings on the neuropsychological tests, neuropsychological impression score, or Kurtzke scale score of neurological signs.

The mean urinary free cortisol level for the 112 HIV-positive men was 61.7±34 μg/24 hours; for the 75 HIV-negative men it was 57.9±27 μg/24 hours. The difference is clearly not statistically significant.

There was no statistically significant difference in urinary free cortisol level between the 21 HIV-positive subjects with any current *DSM-III-R* axis I disorder (70.9±50.2 μg/24 hours) and the 91 without current axis I disorders (55.6±28.5 μg/24 hours) (t=0.99, df=23, n.s.). The seven men with current depression (major depression, dysthymia, or depression not otherwise specified) had a nonsignificantly higher mean urinary free cortisol level (84.8±74.2 μg/24 hours) than the 105 nondepressed subjects (60.2±29.2 μg/24 hours) (t=0.87, df=6, n.s.).

Table 3 shows the correlations for each group between urinary free cortisol level and the 11 planned variables. None of the correlations was significant within the HIV-negative group. Within the HIV-positive group, however, four of the 11 correlations reached statistical significance: symptom checklist score, medical stage, Hamilton depression scale score, and Hamilton anxiety scale score.

DISCUSSION

We found a small but statistically significant relationship between 24-hour urinary free cortisol level and two psychiatric states—anxiety and depression. There was no relationship, however, between cortisol secretion and the most critical immunological markers of HIV infection progression—the numbers of CD4+ and CD8+ T lymphocytes and the CD4-CD8 ratio.

Correlational analyses do not yield causal inferences. Nevertheless, a reasonable interpretation of these data might be as follows: subjects with HIV infection with the most evidence of medical complications may also be the most anxious and depressed. Such patients may show the most evidence of HPA activation with the highest 24-hour urinary free cortisol levels, although the overall degree of HPA activation in our group was minimal. HPA activation does not, however, produce an overall increase in the loss of T helper cells. Thus, stress-induced HPA activation does not seem to cause loss of CD4+ T lymphocytes beyond that already caused by infection itself in early HIV infection.

Several features of our study design and subjects must be noted. First, the overall levels of psychopathology, anxiety, and depression in this group of subjects were low. The mean Hamilton depression scale score of our HIV-positive group was only 4.4, only seven of the 112 HIV-positive subjects met criteria for current depression, and the mean Hamilton anxiety scale score was only 4.0. Severity of depression has been related to degree of immunocompromise (20). It is possible that a group of more depressed or anxious HIV-infected subjects would show even more evidence of HPA activation to the point of provoking glucocorticoid levels high enough to cause immunosuppression.

Second, these subjects were generally not far along in the course of HIV infection. Most of the men in the HIV-positive group were entirely asymptomatic or had only lymphadenopathy. By study design, none of them had the serious opportunistic infections or secondary tumors that define AIDS. Again, we do not yet know if glucocorticoids produce further immunosuppression in patients with more advanced medical disease.

Third, we did not measure the functional capacity of T lymphocytes, only their number. Although the loss of CD4+ T lymphocytes is the hallmark of progressive HIV disease and is probably responsible for many of the protean manifestations of this illness, it is possible that glucocorticoids have an adverse effect on the function rather than the number of these cells early in the disease.

Many of the questions raised will be better answered as we study this group of subjects over time. This will give us an opportunity to see whether advancing signs of HIV infection produce more evidence of HPA activation. At present, we can tentatively assert from this study that stress does not appear to operate through the HPA axis to produce clinically significant immunocompromise among patients with HIV infection. We feel strongly that the prompt and humane treatment of the psychological and psychosocial manifestations of HIV infection is imperative nonetheless.

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APPENDIX 1. Stages of HIV-Related Physical Symptoms

Note: Only physical symptoms assumed to be related to HIV infection are considered. Neurological, neuropsychological, and psychological symptoms are not considered and may be present at any stage.

0–9 Seropositive, physically asymptomatic, i.e., no physical symptoms assumed to be related to HIV infection that in themselves are severe enough to warrant clinical attention.

10–19 Seropositive, limited symptoms only: history or evidence of generalized lymphadenopathy or any clinically significant physical symptoms not meeting criteria for stage IV (e.g., diarrhea for 2 weeks, fever for 2 weeks, fatigue every other day for 1 month).

Describe symptoms: ____________

20–29 Seropositive, serious physical symptoms: history or evidence of any of the following:

____ Oral or esophageal thrush
____ Night sweats for more than 30 days
Duration: ____
____ Fever for more than 30 days
Duration: ____
____ Weight loss greater than 10% of body weight
Percent: ____
____ Diarrhea for more than 30 days
Duration: ____
____ Fatigue for more than 30 days
Duration: ____
____ Oral hairy leukoplakia pulmonary tuberculosis
____ One episode of salmonella septicemia
____ Pneumococcal bacteremia
____ Herpes zoster
____ Hemophilus influenza bacteremia
____ Idiopathic thrombocytopenic purpura

30–39 AIDS, i.e., seropositive, with any of the following:

____ Opportunistic infections: ____________
____ Secondary cancer: ____________

APPENDIX 2. 20-Item Symptom Checklist for HIV Infection

1. Oral candidiasis (ever)
2. Lymphadenopathy/thrush (by examination, currently)
3. Nonallergic body rash (history of, during the last 3 months)
4. Shingles (history of, during the last 3 months)
5. Sinusitis (history of, during the last 3 months)
6. Oral leukoplakia (by examination, currently)
7. Fever (history of, during the last 3 months)
8. Night sweats (history of, during the last 3 months)
9. Rashing or scaling around the eyes (history of, during the last 3 months)
10. Diarrhea (history of, during the last 3 months)
11. Psoriasis (history of, during the last 3 months)
12. Shortness of breath (history of, during the last 3 months)
13. Easy bruising (history of, during the last 3 months)
14. Sore throat (history of, during the last 3 months)
15. Persistent cough (history of, during the last 3 months)
16. Meningitis (history of, during the last 3 months)
17. Hair loss (history of, during the last 3 months)
18. Pneumonia (history of, during the last 3 months)
19. Herpes (oral/genital) (ever)
20. Weight loss (more than 10%) (history of, during the last 3 months)

Family Interactions Within Incest and Nonincest Families

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Objective: The study addressed the questions, What are the interactional patterns in families in which incest occurs? and Do these patterns differ from those of families with other clinical problems? Method: The families for the study were chosen from two outpatient clinics; the C. Henry Kempe National Center for the Prevention and Treatment of Child Abuse and Neglect provided access to families with incest, and the nonincest families each had a child seen in a university child psychiatry clinic. In each of these settings, 30 families were selected in the order of referral for evaluation. All families agreed to participate. Each family was given two tasks to perform during a structured interview. The interviews were videotaped, and 15–20-minute segments were rated independently by two of the authors, who used the Beavers-Timberlawn Family Evaluation Scale to assess interactional behaviors within each family. Results: The incest families were significantly more dysfunctional in all but one area of family interaction. The distribution of power within a family did not differentiate the two types of families. Conclusions: The incest families' dysfunctional patterns that seemed to support and maintain the incestuous behavior were a rigid family belief system, a dysfunctional parental coalition, parental neglect and emotional unavailability, and the inability to nurture autonomy in family members.

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To some degree, all studies of incest must attempt to explain a family system that allows and tolerates the sexual abuse of a child. The literature on child sexual abuse (1–5) is replete with psychodynamic and anecdotal descriptions of relationships in families in which incest occurs. To our knowledge, there have been no published reports of systematic or direct observational studies of patterns of interaction in incest families. Williams and Finkelhor (6), however, reviewed and analyzed several unpublished studies that examined interactions in incest families.

Studies of family interactions (7–10) have provided means for assessing the characteristics of family functioning. In particular, the Beavers-Timberlawn Family Evaluation Scale (7) rates a family's functioning along a health-pathology continuum by looking at variables related to a family's power structure, mythology (perception of reality), skill in negotiating, promotion of autonomy, and handling of affect. When the Beavers-Timberlawn scale was constructed, interrater reliability was established first, and then each of the 13 interaction scales was correlated with an independent rating of overall family health/pathology. The scale correlations ranged from 0.30 to 0.79 across a spectrum of 103 families, who ranged from high levels of competence to severe dysfunction. Each of the correlations was significant in predicting overall functioning at a probability level of <0.005 (7).

It is obvious that incest families are different from "normal," nonclinical families. But to what extent do the patterns of interaction in incest families differ from the patterns found in families with other clinical problems? The Beavers-Timberlawn scale was used to assess interactional behaviors within 30 incest families and 30 families that each included a child seen in a child psychiatry clinic. The purpose of the study was to quantify and clarify interactional patterns in incest families.

METHOD

Subjects

The C. Henry Kempe National Center for the Prevention and Treatment of Child Abuse and Neglect, in Denver, provided access to incest families. The nonincest families were studied at the Child Psychiatry

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Clinic, University of Colorado Health Sciences Center. The two clinics are public facilities that, for the most part, provide treatment services to families with lower socioeconomic status. In each of these settings, 30 families were selected for study in the order of their referral for evaluation and treatment. All of the families selected agreed to participate. The parents signed consent forms for themselves and for their children. Before the incest families became involved in the study, the allegations of sexual abuse were investigated and substantiated by the department of social services; most of these families were mandated into treatment by the legal system. Most of the nonincest families were referred and encouraged to seek treatment by school counselors or social service workers, but their treatment was not mandatory.

The differences between the incest and nonincest families in race, marital status, and socioeconomic status were not statistically significant. Most of the families were white: incest, 27 (90%); nonincest, 25 (83%). The number of couples who were married or had de facto marriages was 12 in the incest group (40%) and 10 in the nonincest group (33%). The number of divorced or separated couples was 18 in the incest group (60%) and 20 in the nonincest group (67%). It is likely that the numbers on marital status for the incest group were affected by the court-ordered removal of some of the abusing parents from their homes. Otherwise, the number of married couples in the incest group might have been considerably higher. Socioeconomic status was determined with the Hollingshead Two-Factor Index of Social Position (11). Most of the families were from socioeconomic levels IV and V: incest, 25 (83%); nonincest, 23 (77%).

Procedure

In this study, incest was defined as inappropriate sexual contact between a child and a parent, stepparent, or grandparent. Sexual abuse included vaginal and anal intercourse, oral-genital contact, mutual or forced masturbation, fondling, and the forced use of enemas. Sexual abuse occurred between the following family members: father and daughter (14 families), stepfather and stepdaughter (11 families), father and son (three families), mother and son (one family), and grandfather and granddaughter (one family). The children in the nonincest families had a wide variety of emotional and behavioral disorders, but there were no active legal charges and no clinical evidence of sexual or physical abuse.

Videotapes of the initial, 50–60-minute structured interviews documented the families' interactions. During the interview, the family was presented with two separate but related tasks. As the first task, family members were asked to give their understanding of the problems that had brought them into treatment. As the second task, they were directed and encouraged to discuss among themselves the problems they had identified. Two of us (P.G.M. and S.V.S.) independently rated 15–20-minute segments of the family interviews using the Beavers-Timberlawn Family Evaluation Scale (7), which assesses family functioning on a continuum of competence. The readily identifiable nature of child sexual abuse precluded blind ratings of the interviews with the incest families. Therefore, whether a family belonged to the incest or nonincest group was known to the raters.

TABLE 1. Differences on the Beavers-Timberlawn Family Evaluation Scale Between 30 Incest Families and 30 Nonincest Families

	Mann-Whitney U Test[a]	
Variable	U	p
Family power structure		
Power	363.5	n.s.
Coalitions	301.0	<0.05
Closeness	237.5	<0.01
Family mythology[b]	72.0	<0.001
Family negotiation	133.5	<0.001
Family autonomy		
Clarity	140.5	<0.001
Responsibility	76.5	<0.001
Invasiveness	202.5	<0.001
Permeability	87.0	<0.001
Family affect		
Expressiveness	129.0	<0.001
Mood	298.0	<0.05
Conflict	84.0	<0.001
Empathy	101.0	<0.001

[a] Two-tailed p.

[b] N=59.

Interrater agreement on the scale's 13 interactional variables and on the global family health/pathology assessment was determined by means of the Spearman rank-order correlation. The Spearman correlations on the 13 variables ranged from 0.43 to 0.83, and the health/pathology assessments correlated at 0.94. Each of the correlations was significant at $p<0.001$ (one-tailed).

The Mann-Whitney U test was used to ascertain differences between the mean scores of the incest and nonincest families. Discriminant analysis was used to determine if all 13 variables on the family evaluation scale distinguished between the two groups of families.

RESULTS

Family Interaction

As shown in table 1, there were significant differences between the incest and nonincest families on 12 of the 13 family interaction variables. Ratings of these interaction patterns on the Beavers-Timberlawn Family Evaluation Scale placed most of the incest families in the "severely dysfunctional" range. Family functioning in the majority of the nonincest families fell within the "mild to moderately dysfunctional" range.

With regard to the overt power structure within the family, more of the parents in the incest families were rated as exhibiting dominance-submission patterns, but the difference was not significant. Parental coalitions, which are a measure of power but promote healthy family functioning, were rated as weaker and less effective in incest families. A few rigid, destructive parent-child coalitions were found in both groups. Most of the incest families were rated as having indistinct boundaries between individuals, while the boundaries in the nonincest group showed flexibility in allowing for appropriate closeness and distance among family members.

"Mythology" refers to the family members' shared belief of how they function as a group. It is a measure of the degree of congruence between the family's belief and the actual behaviors observed by the raters. Members of the incest families were perceived as having incongruous beliefs about themselves and their families. Members of nonincest families were found to be more objective in their beliefs about family functioning, and they essentially saw themselves as they were seen by the raters.

"Negotiation" measures the family's ability to constructively solve problems. The incest families were extremely inefficient in their negotiations and differed significantly from the nonincest families, who had mild to moderate difficulties in problem solving.

The two groups of families were seen as quite different with regard to the variables affecting the development of family members' autonomy: "clarity," "responsibility," "invasiveness," and "permeability." Members of the incest families were significantly less clear in their communications and self-disclosures and were less likely to accept responsibility for their actions, feelings, and thoughts. There was a pervasive pattern of invasive statements in the incest families; family members were told how to act, feel, and think. In the nonincest families, these invasive statements did not reach the same frequency or intensity. In regard to permeability (openness to others), the incest families were significantly less open and responsive in their communications.

The incest and nonincest families were found to differ significantly on the four variables measuring affect: "expressiveness," "mood," "conflict," and "empathy." The range of feelings in the incest families was constricted, and the feelings were frequently masked. In contrast, there was a wider range of feelings in the nonincest families, and they frequently expressed them directly despite obvious discomfort. The ratings of mood or feeling tone for the incest group were clustered on the "cynical and hopeless" end of the scale, whereas the ratings for the nonincest group were distributed along the scale's full range. Most of the incest families were rated as avoiding or obscuring conflict; the nonincest families showed varying degrees of ability in dealing with unresolved conflict. There was a distinct absence of empathic responses in incest families. The nonincest families made numerous attempts at empathic involvement, although they had difficulty in maintaining such a stance.

Global Health and Pathology

After the rating of a family's interaction patterns, the Beavers-Timberlawn Family Evaluation Scale calls for the rater to make a global assessment of the family on a 10-point scale. The incest group was significantly more dysfunctional, according to the Mann-Whitney U Test ($U=19.5$, $N=60$, $p<0.001$, two-tailed).

Discriminant Analysis

The aggregate of variables on the Beavers-Timberlawn scale was used to predict membership for each of the study's 60 families. The percent of families correctly classified was 95%. Group membership was correctly predicted in 29 (97%) of the incest families and 28 (93%) of the nonincest families.

DISCUSSION

Our current knowledge of incest comes from a variety of perspectives and disciplines. This body of literature has yet to be integrated into a comprehensive, multifactor analysis of child sexual abuse. Studies have primarily focused on the incest victim, the perpetrator, and the family. To our knowledge, there have been no systematic studies to clarify the multiple clinical impressions of incest family interactions. Therefore, we attempted to quantitatively assess observable interactions in incest families. The incest families were found to be severely dysfunctional in their patterns of interaction. This finding supports much of the incest literature, but our findings do not support the long-held clinical impression that the dominance-submission power structure is a key pattern in incest families (3–5).

This study has several limitations. First, the two groups were not closely matched. Although referred and encouraged to seek treatment by outside agencies, most of the nonincest families entered treatment voluntarily. All of the incest families were legally required to be evaluated. Therefore, as a comparison group, the nonincest families with children who had clinical conditions were less than optimal, but they provided a better comparison than would have "normal" families.

Second, incest evaluation ethically and legally necessitates the involvement of social service agencies and the legal system. We could not determine how family interaction patterns were specifically affected by outside interventions, but it was our clinical impression that the behaviors observed were entrenched and automatic and persisted despite the outside interventions and the families' knowledge that they were being videotaped. These apparently ingrained behaviors suggest chronic interactional patterns, as opposed to acute behavioral changes.

Third, the incest families' discussions of incest and related matters precluded a blind study.

Despite these limitations, we believe our study adds to the understanding of how incest behavior is tolerated, supported, and maintained within the family. A striking finding was the extent of distortion and incongruence in the belief systems of the incest families. This distorted perception of family functioning appeared to take precedence over and necessitate denial of individual family members' actual feelings, emotional availability, and ability to resolve conflict. These distorted views also seemed to impair family functions that promote healthy individual maturation and autonomy. The perceptions of individual family members were frequently not validated and, if spoken, were ridiculed, rejected, or ignored.

These deficits in family functioning are consistent with findings and clinical observations on the long-term impact of sexual abuse on the victim (2, 5, 12, 13). The victim is forced to adopt the distorted family belief system at the expense of validating his or her own experiences and perceptions, and the acceptance of this distorted belief system apparently leads to individual maladaptive defenses, including dissociative states, denial, cognitive dissonance, distortion of reality and of self, low self-esteem, anxiety, and depression. This severely dysfunctional family system also helps explain the difficulty and delay in disclosure.

The literature (3–5) has supported the clinical notion that a parental relationship characterized by dominance and submission has been a major factor in incest. In our study, this factor did not distinguish between incest and nonincest families. Instead, in rating the family power structures, we observed overt destructive coalitions between the parents in incest families, which allowed and tolerated the sexual abuse of the child. This also supports one arm of Finkelhor's current theory that there are four preconditions for perpetration of child sexual abuse (12) in that, given the existence of sexual arousal in the presence of a child, the family power structure, specifically the coalition between parents, does not limit or inhibit the full expression of those impulses.

These dysfunctional coalitions support the incestuous relationship, which epitomizes the extreme deficits in the parental dyad and in the regulation of closeness, or boundaries, between incestuous family members. To the casual observer this inappropriate interaction between parent and child may appear to indicate closeness, but to us, given our detailed observation of emotional neglect, this only underscores the miserable predicament of the incest victim in a dysfunctional family, in which the nonabusing parent is not available and the abusing parent is available only in an inappropriate and destructive manner. Although the scale did not specifically rate inappropriate sexualized attention between parent and child, our clinical observations in this area support the recent research (14) calling attention to this level and style of interaction within incest families.

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Dissociation and Childhood Trauma in Psychologically Disturbed Adolescents

Barbara Sanders, Ph.D., and Marina H. Giolas, M.A.

Objective: To test the hypothesis that dissociation in adolescence is positively correlated with stress or abuse experienced earlier, the authors assessed dissociation in a heterogeneous group of disturbed adolescents and examined the relationship between the degree of dissociation and the degree of reported childhood stress, abuse, or trauma. Method: The subjects were 47 adolescents, 13–17 years old, who were institutionalized for periods of 1–13 weeks in a private mental hospital; 35 were girls and 12 were boys. Participants completed the Dissociative Experiences Scale and a child abuse and trauma questionnaire. The hospital records of 40 of the 47 adolescents were also available. Results: Scores on the Dissociative Experiences Scale correlated significantly with self-reported physical abuse or punishment, sexual abuse, psychological abuse, neglect, and negative home atmosphere but not with abuse ratings made from hospital records. Conclusions: Together with the authors' previous work showing a relation between childhood stress and later dissociation in normal college students, these findings support the view that dissociation represents a reaction to early negative experience and places multiple personality disorder at the extreme end of a continuum of dissociative sequelae of childhood trauma. Researchers should continue to try to identify psychiatric patients with prominent dissociative characteristics or symptoms and attempt to correlate this phenomenology with negative earlier experiences.

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Dissociation, recognized in current psychiatry as a syndrome, is also appropriately seen as a symptom cutting across syndrome boundaries. Disorders defined by dissociative phenomena are classified in *DSM-III* as dissociative disorders, a category in which multiple personality disorder is probably the most striking example. It is known, however, that dissociative symptoms may be present in other diagnostic categories as well—among patients with eating disorders (1) or those suffering from posttraumatic stress disorder (PTSD) (2), for example. Frequent dissociative experiences are also far from unknown among normal college students (3).

Dissociative disorders are believed to develop, in part, in reaction to severe trauma. The well-documented association between multiple personality disorder and child abuse (4–6) supports this view. Much less is known about the role of stressful early experiences in dissociative disorders other than multiple personality disorder or about the relation between trauma and dissociation in other diagnostic categories (with the notable exception of PTSD). We recently found that dissociation in college students is positively correlated with stressful or abusive earlier experiences (3). This finding led us to expect that a relation between dissociation and trauma should exist across various clinical diagnostic groups. This is particularly true if one views multiple personality disorder as the extreme end of a dissociation continuum extending into the normal population (7, 8). To test our hypothesis, we assessed dissociation in a heterogeneous group of disturbed adolescents and examined the relationship between the degree of dissociation in these individuals and the degree of reported childhood stress, abuse, or trauma.

METHOD

The subjects were 47 adolescents, 13–17 years old, who were institutionalized for periods of 1–13 weeks in a private mental hospital; 35 were girls and 12 were boys. The adolescents were recruited and surveyed at

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the time of their admission to the hospital. Three additional patients, two girls and one boy, who agreed to participate in the study were not included because they either failed to finish one of the two experimental inventories or did not follow instructions in doing so.

All subjects were informed in advance that the study concerned particular types of life experiences and that they would be asked about the frequency of these experiences and about their home environment while growing up. They were assured that their answers to these questions would be confidential within the limits of the laws of the state. Written consent was obtained from each subject and from a parent or guardian before the subject's participation.

Participants were asked to complete the Dissociative Experiences Scale and a child abuse and trauma questionnaire. The Dissociative Experiences Scale, which measures the frequency of various types of dissociative experiences, is internally consistent, has high test-retest reliability (0.84 after 4–8 weeks), and has been shown to discriminate patients with multiple personality disorder from patients in several nondissociative clinical groups as well as from normal subjects (7). The subject responds by marking a line for each item to indicate how often (between 0% and 100% of the time) the particular type of event was experienced; the inventory is scored by measuring the length of the line to the mark in millimeters for each item and computing the mean across all 28 items. We omitted item 1 from the questionnaire because it concerns dissociation while driving and many of our subjects were too young to drive. Otherwise, the inventory was administered and scored in standard fashion.

The child abuse and trauma questionnaire elicits perceptions of negative treatment by parents (or principal caretakers) and negative home atmosphere by having the respondent indicate on a 5-point scale how frequently particular events or situations occurred during his or her childhood and adolescence. The response categories are 4=always, 3=very often, 2=sometimes, 1=rarely, and 0=never. The 37 questions cover five general areas of child abuse and trauma: physical abuse or punishment, psychological abuse, sexual abuse, neglect, and negative home atmosphere. Sample questions from each of the five areas are presented in appendix 1. In addition to these five scales, the child abuse and trauma questionnaire contains two questions about the parents' childhood history of physical and sexual abuse, and one omnibus question, "Was your childhood stressful?" which were analyzed separately.

For most of the child abuse and trauma questionnaire items a higher response indicates a more negative home environment. Five of the items, however, are deliberately worded so that a higher response category indicates a more positive environment, and these items are reverse-scored. A subject's score in each of the five scales is the mean of the response values for the items in that scale. The total child abuse and trauma questionnaire score is the mean of the five scale scores.

We had access to the hospital records of 40 of our subjects. The remaining seven, surveyed early in the project, could not be identified from their experimental materials because of a coding problem that was rectified as data collection proceeded. The patient records, including the psychotherapists' notes and summaries of family background and social history, were used to reach an independent assessment of the extent of abuse or trauma experienced by each subject. Ratings were made by one of us (M.H.G.), who was blind with respect to the child abuse and trauma questionnaire and Dissociative Experiences Scale scores when making the judgments. Each subject was given an overall rating of 0–4 indicating the degree of physical abuse, psychological abuse, sexual abuse, neglect, and negative home atmosphere. A second rating, concerned specifically with sexual abuse, was also made for each subject. This rating was made on a 3-point scale (finer discriminations were not meaningful) on which 0=no mention of sexual abuse, 1=sexual abuse present, and 2=chronic or extremely severe sexual abuse. To establish the reliability of these ratings, a trained research assistant also rated overall abuse and sexual abuse for 38 of the subjects. Interrater agreement for the overall abuse rating was 79%; seven of the eight disagreements involved adjacent categories (kappa=0.72). Interrater agreement for sexual abuse ratings was 100% (kappa=1.00).

The hospital charts were also consulted for the subject's clinical diagnosis; the primary *DSM-III-R* diagnosis at time of discharge was recorded.

RESULTS

One subject did not answer any of the items on the child abuse and trauma questionnaire sexual abuse scale and was therefore not included in analyses involving this scale. The total child abuse and trauma questionnaire score for this subject was considered to be the mean of the four other child abuse and trauma questionnaire scale scores.

The Guttman split-half reliability of the child abuse and trauma questionnaire was 0.86. Scores on the five scales were positively intercorrelated and, with one exception (a correlation of 0.19, p=0.10, between the punishment and sexual abuse scales), all intercorrelations were statistically significant. There were no sex differences on any of the child abuse and trauma questionnaire scales.

Responses to the single global question, "Was your childhood stressful?" correlated significantly with all five child abuse and trauma questionnaire scale scores and correlated at 0.88 with the overall child abuse and trauma questionnaire score.

The frequency of physical and sexual abuse experienced by the parents, as reported by the adolescent subjects, correlated significantly with the child abuse and trauma questionnaire psychological abuse, sexual abuse, and negative home atmosphere scale scores and with the overall child abuse and trauma questionnaire score. In all cases, the greater the abuse the parents had experienced, the more negative the environment they provided for their children. This finding provides additional evidence for the transgenerational nature of abuse.

The distribution of Dissociative Experiences Scale scores was positively skewed: the mean±SD score was 19.2±15.0, the median was 14.6, and the range was 0.44 to 61.9. The scores of the boys did not differ significantly from those of the girls.

Scores on the Dissociative Experiences Scale correlated positively and significantly with scores on each of the five child abuse and trauma questionnaire scales. Correlations ranged from 0.26 for sexual abuse to 0.50 for negative home atmosphere. The correlation between the Dissociative Experiences Scale scores and the total child abuse and trauma questionnaire scores was 0.44 (df=45, $p<0.001$); the correlation between the Dissociative Experiences Scale scores and the single question, "Was your childhood stressful?" was 0.31 (df=45, p=0.02).

Correlational analyses between the hospital chart ratings and the scores on the five child abuse and trauma questionnaire scales showed that the ratings of overall abuse or trauma based on the charts correlated with the sexual abuse scale scores of the child abuse and trauma questionnaire (r=0.38, df=37, $p<0.01$) and with responses to the child abuse and trauma questionnaire question, "Was your childhood stressful?" (r=0.33, df=38, p=0.02). The correlation between the abuse or trauma rating based on the charts and the total child abuse and trauma questionnaire scores, however, did not quite reach statistical significance (r=0.24, df=38, p=0.06). Ratings of sexual abuse based on the hospital charts were significantly correlated with the sexual abuse scale scores of the child abuse and trauma questionnaire (r=0.50, df=37, $p<0.001$).

In contrast to the positive findings obtained with the child abuse and trauma questionnaire scales, correlations between the chart ratings of the environment and the Dissociative Experiences Scale scores were statistically nonsignificant and negative: for overall abuse or trauma, r=−0.16, df=38, p=0.17; for sexual abuse, r=−0.21, df=38, p=0.10).

The *DSM-III-R* diagnoses of the 40 subjects for whom this information was available were mood disorder (depression or dysthymia), N=12; conduct disorder, N=10; adjustment disorder, N=5; PTSD, N=2; schizophreniform disorder, N=2; attention deficit disorder, N=1; eating disorder, N=1; oppositional disorder, N=1; substance abuse disorder, N=1; impulse control disorder, N=1; parent-child problem, N=1; personality disorder, N=1; and diagnosis uncertain, N=2. Although the numbers of subjects with each diagnosis are too small to allow systematic comparisons of Dissociative Experiences Scale scores among diagnostic categories, it is noteworthy that patients with high Dissociative Experiences Scale scores were dispersed across these various diagnostic groups. For example, the diagnoses of the nine individuals with the highest Dissociative Experiences Scale scores (greater than 30) were mood disorder (N=2), attention deficit disorder (N=1), eating disorder (N=1), conduct disorder (N=2), personality disorder (N=1), adjustment disorder (N=1), and substance abuse disorder (N=1).

DISCUSSION

The principal finding of this study is that the child abuse and trauma questionnaire, our self-report inventory of child abuse and trauma, correlated significantly with the frequency and extent of dissociative experiences as indexed by the Dissociative Experiences Scale. The degree of dissociation in this group of adolescents was related to their scores on all five of the child abuse and trauma questionnaire scales: physical abuse or punishment, sexual abuse, psychological abuse, neglect, and negative home atmosphere. Although these correlations were all statistically reliable, most were of modest magnitude. The correlation of 0.44 between the overall child abuse and trauma questionnaire scores and the Dissociative Experiences Scale scores reflects a shared variance of approximately 19%.

The extent of dissociation in the adolescent patients can be appreciated by comparing their Dissociative Experiences Scale scores with those of the college students in our earlier investigation (3) and with clinical groups surveyed by Bernstein and Putnam (7). The adolescents in the present study scored slightly higher than the college students, who had a median score of 11.2 (N=309). Although the shape of the frequency distribution was essentially the same in the two groups and the range of scores was comparable, there were proportionally more high scores among the adolescents in the current study. For example, 11 (23%) of our 47 adolescent patients had Dissociative Experiences Scale scores above 31.2, the median for patients with PTSD in Bernstein and Putnam's study, but only 8% of the college students in our earlier study had scores this high. The median Dissociative Experiences Scale score achieved by Bernstein and Putnam's patients with multiple personality disorder was 57, a value at the outside edge of the distribution in both of our studies: just one of the 646 college students in our earlier study exceeded this score (with a score of 62.3), and one disturbed adolescent in the current study did so (with a score of 61.9). In evaluating the degree of dissociation in these study groups, it should be noted that dissociative experiences decline during adolescence and may not have precisely the same meaning in adolescents as they do in adults (7, 9).

The variability of Dissociative Experiences Scale scores is as noteworthy as their magnitude. In the present sample this variation was considerable and was not related in any obvious way to diagnosis. Variability among diagnostic categories is attested to by the fact that the nine highest-scoring patients with a known diagnosis were from seven different diagnostic categories. Variation within a diagnostic group, although more difficult to document in our data because of the small numbers of patients with each diagnosis, was nonetheless evident in the two diagnostic groups with at least 10 patients: mood disorder and conduct disorder. Both had sizable ranges (5–60 for mood disorder, 1–52 for conduct disorder) and large standard deviations.

The suggestion that *DSM-III* diagnostic groups may be heterogeneous in dissociation is supported by Ross and Anderson's observations of phenomenological variation in obsessive-compulsive disorder in adults (10). These investigators found that during Amytal interviews conducted with three obsessive-compulsive disorder patients, two patients entered a dissociative state in which a separate-personality-like entity was revealed who claimed responsibility for the patient's obsessions and compulsions. The third obsessive-compulsive patient did not dissociate during the interview. The Dissociative Experiences Scale clearly distinguished the nondissociative obsessive-compulsive patient (her Dissociative Experiences Scale score was 5.2) from the other two, each of whom had Dissociative Experiences Scale scores of approximately 30. These researchers suggested that patients with dissociative obsessive-compulsive disorder may be a psychologically and biologically distinct subgroup on a continuum with patients with multiple personality disorder. It is possible that other diagnostic categories also contain distinct subgroups whose members share prominent dissociative characteristics.

Although the Dissociative Experiences Scale scores were positively correlated with the child abuse and trauma questionnaire scores in our study, they were not related to abuse ratings based on hospital records. There are several possible explanations for this. Since the adolescents were hospitalized for relatively brief periods of time, the records were based on limited information and may have been less accurate than the child abuse and trauma questionnaire inventory. Also, patients may have felt freer to respond truthfully in a research project than to a therapist or hospital authority figure, again suggesting that the child abuse and trauma questionnaire may give a more accurate reflection of trauma or abuse. It may also be important that the child abuse and trauma questionnaire assesses the adolescent's own view of the stressfulness of his or her home life (e.g., "Did you feel safe living at home?") and includes some fairly everyday types of events (e.g., "Were your parents unwilling to attend any of your school-related activities?"), whereas the chart records highlight more dramatic incidents with no direct measure of their impact on the patient. Any or all of these variables may be responsible. There is another quite different possibility: perhaps it is those negative home experiences which have not become part of the adolescent's routinely given family history that are critically related to dissociative phenomena. In other words, perhaps it is the stress generated by events not talked about, or at least not talked about early in treatment, that triggers dissociation. Whatever the reason or reasons for the difference, the fact that positive findings were obtained with the child abuse and trauma questionnaire and not with the routinely kept hospital records suggests that clinicians interested in family background information which might be indicative of dissociation consider the early use of a structured self-report measure such as the child abuse and trauma questionnaire to index abuse and trauma.

Our work so far has established a relationship between degree of dissociation and degree of childhood stress in this mixed psychiatric sample and in normal college students. These findings place the phenomenon of multiple personality disorder, with its origins in early overwhelming physical, sexual, and psychological abuse, at the extreme end of a continuum of dissociative sequelae of childhood stress. Not since Freud's earliest proclamations about the origin of hysteria have traumatic childhood experiences been regarded as having such specific consequences for psychological development. In order to establish the specificity of the relation between abuse and dissociation, researchers should continue to try to identify psychiatric patients with prominent dissociative characteristics or symptoms and attempt to correlate this phenomenology with negative earlier experiences. In adolescents, the diagnostic categories of mood disorder and conduct disorder may be particularly interesting ones in which to conduct such investigations. The considerable variability in dissociation that we observed in these latter two diagnostic groups, coupled with the fact that victims of child abuse frequently meet diagnostic criteria for these categories (11), encourages our expectation that these diagnostic categories may contain subgroups of patients with high levels of dissociative experiences and childhood histories of physical and psychological traumata.

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APPENDIX 1. Sample Items From the Child Abuse and Trauma Questionnaire Scales

Physical abuse and punishment:
- When you didn't follow the rules of the house, how often were you severely punished?
- Were you physically mistreated as a child or teenager?

Psychological abuse:
- Did your parents ridicule you?
- Did your parents ever verbally lash out at you when you did not expect it?

Sexual abuse:
- Were there traumatic or upsetting sexual experiences when you were a child or teenager that you couldn't speak to adults about?
- Did you ever have reason to fear alcohol-influenced sexual mistreatment from either of your parents?

Neglect:
- As a child did you feel unwanted or emotionally neglected?
- As a child did you have to take care of yourself before you were old enough?

Negative home atmosphere:
- Did your parents verbally abuse each other?
- Did you ever think you wanted to leave your family and live with another family?

Psychiatric Morbidity in Adult Inpatients With Childhood Histories of Sexual and Physical Abuse

George R. Brown, M.D., and Bradley Anderson, M.D.

Objective: To extend the knowledge on long-term effects of childhood abuse in psychiatric patients to a large sample, the authors explored childhood sexual and physical abuse in adult inpatients over 1,040 consecutive admissions. Method: The 947 patients were admitted to a tertiary-care military medical center. Each patient was interviewed, and abuse history, DSM-III-R diagnosis, and other characteristics were recorded. Results: The prevalence of reported childhood abuse was 18% overall: 9% for sexual abuse (with or without physical abuse), 10% for physical abuse (with or without sexual abuse), and 3% for combined abuse. More female than male patients reported abuse. Alcohol use disorders were more common in victims of physical or combined abuse than in sexually abused or nonabused patients. Axis II diagnoses, particularly borderline personality disorder, were more frequent in abuse victims than in nonabused patients. Histories of drug and alcohol abuse were more common in patients reporting physical or combined abuse than in nonabused patients. Suicidality was also more frequent in abused than nonabused inpatients and was noted in 79% of the patients with histories of combined abuse. Combined abuse in women and physical abuse in men were associated with a family history of psychiatric illness, most commonly alcoholism in male relatives. Conclusions: These findings emphasize the need for greater attention to family dynamics, aggressive diagnosis and treatment of alcoholism within the family, and, especially, determination of patients' abuse histories, even if repeated questioning is necessary.

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Mental health professionals are becoming more aware of the possibility of sexual and physical abuse in the histories of patients requesting treatment in a variety of clinical settings (1–3). This awareness is based on a burgeoning, largely descriptive literature on child abuse and its potential sequelae and on increased media attention to incest, rape, battering, and domestic violence. However, in the last decade, few studies have examined the childhood abuse histories of general adult psychiatric inpatients. Jacobson and Richardson (4) conducted one of the few studies with a contemporaneous interview design. Of their 100 psychiatric inpatients, 57% reported that they had been victims of either sexual or physical abuse before admission. Carmen et al. (5, 6) investigated the abuse experiences of 188 psychiatric inpatients using retrospective chart review techniques, and they found that 43% reported histories of abuse. With the exception of these studies, most examinations of adult psychiatric inpatients have focused on the childhood abuse of female patients only (7–10), a limitation that is unfortunate given the growing recognition that males are sexually abused far more frequently than was once believed (11).

Several studies have examined specialized psychiatric inpatient samples, e.g., male alcoholic patients in a Veterans Administration hospital (12, 13) and opiate addicts in the inner city (14). Studies of the long-term effects of childhood sexual abuse on adult outpatients have been reviewed elsewhere (1, 15).

In spite of the plethora of descriptive papers regarding the putative long-term effects of childhood sexual and physical abuse on adult psychological functioning, the study of such sequelae is in its infancy. Few studies have involved large samples, and many did not use valid comparison groups, making their results impos-

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sible to interpret. To our knowledge, no studies have compared *DSM-III-R* psychiatric diagnoses in a large sample of abused and nonabused general adult psychiatric inpatients.

Methodological problems notwithstanding, clinicians recognize that abused individuals seeking treatment may display characteristic symptoms that need to be addressed in any successful psychotherapeutic intervention. For example, many exhibit chronic self-destructive behavior, poor self-esteem, anxiety, feelings of isolation, sexual maladjustment, and interpersonal dysfunction (15, 16). Other investigators (4, 5, 8) have called for routine inquiry into patients' histories of physical and sexual abuse to address how widespread these clinical findings are and to fill the large gaps in empirical knowledge.

Our study answers the call for routine inquiry. We report on what we believe to be the largest group of consecutively admitted, adult psychiatric inpatients to be routinely interviewed for childhood histories of physical and sexual abuse (1,019 admissions). *DSM-III-R* psychiatric diagnoses, drug and alcohol use patterns, suicidality, family history data, length of stay, and demographic characteristics of adult inpatients with self-reported histories of abuse were compared to corresponding data for nonabused inpatients from the same treatment unit. Associations between specific diagnoses and a history of abuse have been suggested in previous studies of small groups of inpatients (3, 17, 18). We addressed these associations but used a much larger patient sample.

METHOD

Sample

Wilford Hall Medical Center is the U.S. Air Force's largest tertiary-care medical center. Active-duty and retired military members from all branches of the armed services and their dependents are entitled to care. Patients consecutively admitted to one of two identical 30-bed psychiatric wards were each routinely queried during one or more interviews regarding history of physical and sexual abuse, and these data were entered into a prospectively maintained data base along with demographic variables, admission and discharge diagnoses, past and family psychiatric histories, medications, treatment outcome, and disposition (19). This study used no retrospective chart review data. We logged 1,040 consecutive admissions between Sept. 1, 1987, and Oct. 1, 1989; 21 records (2%) were incomplete and were excluded from analyses, yielding 1,019 records on 947 different patients. A low rate of readmission is characteristic of this medical center: 63 patients were admitted twice during this 25-month period, eight patients were admitted three times, and one patient was admitted four times. The mean length of stay in this unit was 13 days, and no patient stayed longer than 95 days.

Because patients frequently responded differently to abuse questions at different admissions, multiple admissions were treated as separate patients; unless otherwise specified, all numbers and percentages involving patients refer to admissions (1,019).

In our sample, 66% of the admitted patients were on active duty at the time of evaluation (N=673), and 34% were civilians (N=346); 18% (N=188) were admitted during basic military training at Lackland Air Force Base. Because the latter group represents a highly specific subpopulation, even in the military setting, duplicate analyses were performed. All branches of the armed services were represented.

Over half of the subjects were men (59%, N=601). Seventy-two percent were white (N=734), 14% were black (N=141), 8% were Hispanic (N=85), and 6% were Asian (N=59). The average age of the sample was 30 years (median=25 years, range=17–90). The proportions of married and single patients were equal (45%, N=459); 7% were divorced (N=71), and 3% were widowed (N=31).

The majority of the patients were employed, attending college, and/or receiving retirement benefits. A minority were considered to have low socioeconomic standing, and less than 1% were classified as homeless and mentally ill.

Procedure

Each patient was evaluated by at least one of two Board-certified psychiatrists on the faculty of the Wilford Hall Medical Center psychiatry residency training program. The interrater diagnostic differences for primary axis I diagnoses were found to be negligible (less than 5%) for 40 paired, blind assessments of the same inpatients. Each patient was also interviewed by one or more psychiatric residents. All information revealed to interviewers at any time during the hospital stay was used for analysis.

The definition of sexual abuse used in this study was as follows: any self-reported sexual contact—ranging from fondling to sexual intercourse—experienced by a patient on or before age 18 and initiated by someone 5 or more years senior or by a family member at least 2 years senior. This definition includes exploitative sexual contact with minor children between 16 and 18 years of age and incestuous contact between siblings of different developmental ages (16, 20). Furthermore, it encompasses the U.S. National Center on Child Abuse and Neglect's definition of child sexual abuse (any act perpetrated on a child by a significantly older person with the intent to stimulate the child sexually and to satisfy the aggressor's sexual impulses) (21).

Physical abuse was defined as any self-reported assault on or before age 18 that was perpetrated by an assailant 5 or more years senior or an assault by a family member at least 2 years senior that was not interpreted by the patient as an intrafamilial fight, e.g., sibling rivalry. Fights between peers were excluded, as was verbal or psychological abuse in the absence of physical contact. A suspected history of abuse not admitted by the patient was not recorded as an abuse case.

Histories of sexual and physical abuse were elicited by means of sensitive, broad questions, such as, "Before you were 18 years old, did anyone touch you or engage you in a sexual way without your permission?" An affirmative or ambivalent response was followed by a more detailed series of questions to obtain specific recollections of events and the perpetrators, if known. For example, "I realize this may be difficult for you to talk about, but could you tell me who it was? What exactly happened to you? How old were you at the time? Were any other adults involved, or did they know about the incident?" Physical abuse histories were elicited with the question "While you were growing up, before age 18, were you disciplined by anyone in a way that you considered excessive?" Histories of physical abuse without the pretense of discipline were also sought. All abuse experiences that occurred after the age of 18 were excluded. Because of the need for confidentiality and our concern for the safety of the patients, no corroborating evidence was sought for any self-reported case of abuse.

Chi-square analyses with Yates' correction, 2×2 or 2×3, were performed to compare patients in each abuse category (physical, sexual, or combined) with the remainder of the inpatient group, who served as a comparison group. To limit type I error, a significance level of $p<0.01$ was uniformly applied.

RESULTS

Of the 947 patients interviewed, 166 (18%) reported histories of abuse. Sexual abuse (with or without physical abuse) was reported by 86 patients (9%), physical abuse (with or without sexual abuse) was reported by 94 patients (10%), and combined abuse was reported by 28 patients (3%). Physical abuse alone was reported by 70 patients (7%), 41 (59%) of whom were male. Sexual abuse alone was reported by 68 patients (7%), 20 (29%) of whom were male.

More women than men reported sexual abuse (71 versus 25; $\chi^2=48.8$, df=1, $p<0.0001$) and physical abuse (52 versus 46; $\chi^2=6.9$, df=1, $p=0.008$). Of the 28 patients who reported combined abuse, 23 (82%) were women and five were men ($\chi^2=38.3$, df=1, $p<0.0001$). Physical abuse was significantly more common among the 71 sexually abused women than among other female inpatients (32% versus 8%; $\chi^2=30.7$, df=1, $p<0.0001$). In contrast, physical abuse was not significantly more common among the 25 sexually abused men than among other male inpatients (24% versus 7%) ($\chi^2=4.0$, df=1, $p=0.05$).

DSM-III-R psychiatric diagnoses for patients in each abuse category are listed in table 1. In addition to current diagnoses of alcohol use disorders, the patients with physical abuse histories also had a higher prevalence of past alcohol use disorders (N=49) than patients who had not been physically abused (50% versus 32%; $\chi^2=13.0$, df=1, $p=0.0003$). They also had a higher prevalence of illicit drug use during their lifetimes (38% versus 24%; $\chi^2=9.5$, df=1, $p=0.002$). This relationship was not observed for patients who had been sexually abused. The difference in past history of alcohol use disorders between the combined abuse group and the nonabused group approached significance (54% versus 38%; $\chi^2=6.6$, df=2, $p=0.04$). The prevalence of lifetime illicit drug use increased with increasing levels of reported abuse: 23% of the nonabused group (N=200), 30% of those reporting either type of abuse (N=41), and 46% of those who reported combined abuse (N=13) ($\chi^2=9.6$, df=2, $p=0.008$). When the female abuse victims were considered separately, the prevalence of illicit drug use was nearly twice as high in those who reported combined abuse (44%, N=10) than in those with either a physical or sexual abuse history alone (23%, N=18) ($\chi^2=11.9$, df=2, $p=0.003$).

Personality disorders were diagnosed significantly more frequently in all abuse groups than in nonabused patients (table 1). A significant stepwise increase in the proportion of patients with borderline personality disorder was noted with increasing levels of reported abuse: 3% of nonabused patients, 13% of patients with either type of abuse alone, and 29% of those with both types of abuse ($\chi^2=57.3$, df=2, $p<0.0001$). Borderline personality disorder accounted for 48% of all axis II diagnoses in the abused patients.

Suicidality (ideation, recent gesture, or attempt) at admission was examined in all groups. The proportion of patients who were suicidal on admission was significantly higher in the patients with histories of either physical or sexual abuse (75%, N=103) than in the nonabused patients (57%, N=490) ($\chi^2=18.7$, df=2, $p<0.0001$). Suicidality was noted in 79% (N=22) of the patients with combined abuse. Male inpatients with sexual abuse histories were more likely to be suicidal on admission (88%, N=22) than men who did not report sexual abuse (57%, N=329) ($\chi^2=8.4$, df=1, $p=0.004$). There was no significant association between homicidality (ideation, intent, or attempt) and any abuse category.

Family history of major psychiatric illness was significantly more prevalent among abused women than among nonabused women. Fifty-one percent of the nonabused women (N=159) reported positive family histories, whereas 65% of the women who had been either sexually or physically abused (N=50) and 78% of the women with combined abuse (N=18) related such histories ($\chi^2=10.5$, df=2, $p=0.005$). A family history of major psychiatric illness was reported by 48% of the nonabused men (N=261) but was significantly more common in the men with histories of physical abuse only (89%, N=41; $\chi^2=27.4$, df=1, $p<0.0001$) or combined abuse (80%, N=4; $\chi^2=26.3$, df=2, $p<0.0001$).

TABLE 1. Diagnoses Given for 1,019 Consecutive Admissions of Psychiatric Inpatients With or Without Childhood Histories of Physical and/or Sexual Abuse[a]

	Physical (N=98)		Sexual (N=96)		Combined (N=28)		None (N=853)	
DSM-III-R Diagnosis	N	%	N	%	N	%	N	%
No diagnosis	2	2	1	1	0	0	26	3
V codes	68	—	63	—	19	—	398	—
Axis I diagnoses	107	—	94	—	35	—	931	—
Adjustment disorder	29	30	28	29	6	21	272	32
Alcohol use disorder	27	28[b]	16	17	12	43[c]	180	21
Other substance use disorder	15	15	11	11	5	18	55	6
Major depression	8	8	4	4	1	4	53	6
Dysthymia	2	2	5	5	2	7	17	2
Bipolar disorder	7	7	3	3	2	7	55	6
Anxiety disorder	7	7	4	4	2	7	35	4
PTSD	2	2	3	3	1	4	9	1
Eating disorder	3	3	5	5	3	11	7	1
Organic mental disorder	2	2	2	2	0	0	61	7
Schizophrenia[d]	1	1	1	1	0	0	86	10
Delusional disorder	0	0	2	2	0	0	19	2
Psychosexual disorder	1	1	4	4	0	0	10	1
Axis II diagnoses	32	34[e]	34	40[f]	16	57[g]	179	21
Borderline[h]	13	14	18	21	8	29	26	3
Not otherwise specified	16	17	12	14	8	29[i]	88	10

[a] Some patients were admitted more than once; the numbers in the table refer to numbers of diagnoses. For patients with multiple admissions, repetitions of the same diagnosis were excluded. The physical and sexual abuse categories overlap, i.e., they contain patients who reported both types of abuse. The statistical comparisons refer to differences between the abuse groups and the group with no reported history of abuse.

[b] $\chi^2=12.9$, df=1, p=0.0003.

[c] $\chi^2=8.7$, df=2, p=0.01.

[d] Significantly fewer patients in each abuse category were diagnosed as having any psychotic disorder (schizophrenia, schizophreniform disorder, schizoaffective disorder, psychotic disorder not otherwise specified, brief reactive psychosis) ($\chi^2=17.8$, df=2, p<0.0001).

[e] $\chi^2=13.6$, df=1, p=0.0002.

[f] $\chi^2=16.8$, df=1, p<0.0001.

[g] $\chi^2=31.9$, df=2, p<0.0001.

[h] Significantly more frequent in all abuse categories than in the group with no abuse ($\chi^2=57.3$, df=2, p<0.0001).

[i] $\chi^2=9.0$, df=2, p=0.01.

A complete reanalysis of the data after exclusion of basic trainees (N=188) yielded only minor differences from the data already reported. Seven percent of the trainees (N=14) reported physical abuse, 7% reported sexual abuse (N=14), and 1% reported combined abuse (N=1). All differences in results between the samples including and excluding the basic trainees were at statistical levels greater than p=0.05.

Table 2 lists the relationships of the reported perpetrators of abuse to their victims. Twenty-seven percent of all perpetrators of physical abuse were women (N=32), and only 7% of the sexual abusers were women (N=8). Between 95% (N=114) and 97% (N=116) of the physical abusers were family members (by birth or by law), and 56% (N=69) to 67% (N=83) of the sexual abusers were related to the victim (the maximum figure assumes all "unspecified" perpetrators were family members).

DISCUSSION

To our knowledge, the results reported here are derived from the largest sample of consecutively admitted adult inpatients to be examined systematically for the presence of childhood abuse histories. The prevalence of abuse reported herein (18%) was lower than that in other studies of inpatients (4, 5, 8). The other studies used highly selected samples and exclusion criteria, which may have inflated the prevalence of abuse by preferentially reducing the denominators. For example, Jacobson and Richardson (4) eliminated 58% of the admissions during their 2-month study and Bryer et al. (8) eliminated all male patients and included only 38% of the female patients admitted during their study. Because we excluded only 2% of all consecutive admissions over the 25-month study period, it is conceivable that our rate may be a more accurate reflection of abuse in adult inpatients. If the 189 patients with symptoms of psychosis on admission were eliminated from our study, the prevalence of reported abuse would rise to 19%.

The low rate of abuse in our sample may also be a function of our methods. For example, even though we attempted to collect abuse histories from patients with psychotic disorders only after they were stabilized, the number of affirmative responses may be spuriously low. Other researchers have shown that a high percentage of abused patients in state hospitals who are observed over many months have chronic psychotic

TABLE 2. Perpetrators of Childhood Physical and/or Sexual Abuse Reported by Psychiatric Inpatients[a]

Perpetrator's Relationship to Victim	Physical (N=94)		Sexual (N=86)	
	N	%	N	%
Father	59	63	18	21
Mother	29	31	3	3
Stepfather	14	15	11	13
Brother	5	5	10	12
Sister	2	2	1	1
Uncle	1	1[b]	14	13[b]
Grandparent	2	2	2	2
Foster parent	2	2	3	3
Stepbrother	0	0	2	2
Stepuncle	0	0	2	2
Cousin	0	0	3	3
Unrelated adult[c]	4	3[b]	40	33[b]
Unspecified	2	2	14	11
Multiple abusers	24	25	23	27

[a] The total number of perpetrators was 120 for physical abuse and 123 for sexual abuse. Unless otherwise specified, the numbers in the table refer to numbers of patients.

[b] Percentage of total number of specified perpetrators.

[c] Teacher, stranger, babysitter, or family friend.

disorders (7, 9). Therefore, we may not have an accurate estimate of abuse histories in these patients.

Men may be less likely to reveal their childhood sexual assault experiences to their therapists than are women (4). The higher proportion of men in this study compared to most nonfederal general inpatient settings may lead to higher rates of underreporting if one assumes that males in our culture are less likely to report abuse (22).

Most victims of combined abuse are women. Unlike the situation for males, experiencing one type of abuse appears to be a risk factor for the other in females. Data on family psychiatric history may explain this. In our study, many abused patients came from families with psychiatric illnesses, of which alcoholism appeared to be the most common. Women with histories of combined abuse had the highest percentage of families with psychiatric disorders (78%). Male family members were the most frequent perpetrators of both physical and sexual abuse and were more often identified as problem drinkers and alcoholics by the female inpatients than by the male abuse victims. Alcohol use disorders are frequently reported to exist in perpetrators of child abuse (4, 12, 23) and may be linked to the high rates of combined abuse in girls and physical abuse in boys, both of which were committed most often by fathers or stepfathers. Relative to the incidence of father-daughter incest, father-son incest is rare.

Alcohol use disorders are also common in victims of abuse (5, 14). In our study, this was most striking for the subjects who reported physical abuse alone, who had significantly higher rates of both past and current alcohol use disorders than the nonabused inpatients. This high prevalence may be attributable in part to greater family history of alcoholism, but alcohol abuse itself may in some cases be a nonspecific, but suggestive, adult symptom of childhood physical abuse.

A history of physical abuse is also strongly linked to use of illicit drugs during one's lifetime; the percentage of patients who reported lifetime use of illicit drugs was twice as high for the patients who had experienced combined abuse as for nonabused inpatients. Much of this drug use was reported to have occurred during adolescence, either during the period in which the abuse occurred or shortly thereafter. Although some patients retreat from abusive environments through dissociation (24, 25), multiple personality disorder (26), or somatization (27), it appears that many abused people rely on chemical escape routes, even more frequently than nonabused patients who suffer from other psychiatric illnesses.

Suicidality was not only the most common symptom on admission for abused patients, but it was also much more common in them than it was in nonabused psychiatric inpatients, a population known for having a higher rate of suicidality than the general population. Compared to the nonabused patients, significantly more of the patients with histories of either sexual or physical abuse were suicidal on admission. Combined abuse did not result in an identifiable additive or synergistic effect. Despair, guilt, and self-reproach regarding past abuse were rarely implicated by patients as "reasons" for suicidality. Many of the suicidal abused patients had no accompanying axis I psychiatric disorders and could not identify why they were suicidal, but they noted that this was a chronic, intermittent symptom beginning sometime after they had been abused. Our study extends previous findings (8) of a strong association between childhood sexual abuse and suicidality on admission for female patients to male patients as well.

This study offers dramatic confirmation of the high prevalence of borderline personality disorder in adults who report childhood histories of abuse, which was suggested by others (3, 8, 25). Bryer et al. (8) noted that the only significant finding which spanned all abuse categories in female inpatients who completed the Millon Clinical Multiaxial Inventory was a stepwise increase in the score for borderline personality; nonabused patients scored lowest, sexually abused women scored intermediate, and victims of both physical and sexual abuse scored the highest. On the basis of the frequent difficulties such patients have with trust, it can be hypothesized that many of the patients with borderline personality disorder in the "nonabused group" had actually been abused but they had either dissociated these experiences or chosen not to discuss them with their therapists. Patients in our study did not always report histories of abuse on their first admission. Certainly this line of inquiry should be followed carefully and repeatedly on each admission with patients who meet the criteria for borderline personality disorder. Zanarini et al. (25) have suggested that childhood physical and/or sexual abuse is etiologically important in the development of borderline personality disorder in most patients from disadvantaged backgrounds. Our investigation tentatively extends the probable etiological role of childhood abuse to a sample of largely middle-class inpatients.

The majority of perpetrators of sexual abuse are natural fathers or stepfathers of the victims (10). We found that uncles were more often named as sexual abusers than all other relatives except fathers. In addition to the mothers who were identified as direct perpetrators of sexual abuse, many other mothers apparently knew about their children's abuse, but passive involvement was not recorded as active abuse in this study. The destructive impact of their mothers' passive permission for the abuse was a recurrent theme in the therapy of patients who believed or knew that their mothers did little or nothing to intervene on their behalf. Mothers have rarely been identified as sexual abusers in other studies.

In this study, both physical and sexual abuse were predominantly intrafamilial. Among the reported perpetrators of the childhood abuse, the ratio of fathers to mothers was 6:1 for sexual abuse but 2:1 for physical abuse. Physical abuse by unrelated individuals was rarely reported by the inpatients in our group, whereas at least one-third of the sexual abusers were unrelated to their victims. However, these unrelated abusers were nearly always known to the abused patients and/or their families. Almost three-fourths of all abused patients suffered childhood abuse at the hands of a single adult. Greater attention to family dynamics and direct questioning about current and past abuse are warranted. Alcoholism within the family should be aggressively diagnosed and treated. The importance of eliciting abuse histories from both inpatients and outpatients, even if repeated questioning is necessary, cannot be overemphasized.

Our examination of adult psychopathology in inpatients with abuse histories does not yield a unique symptom complex. However, the following patient profile was found to be commonly associated with a past history of abuse: drug and/or alcohol abuse, suicidality on admission (often chronic), and character pathology (especially symptoms of borderline and self-defeating personality disorders) against a backdrop of family dysfunction and psychiatric illness (often alcoholism in the father or stepfather) and unsuccessful outpatient treatment before admission. This profile is consistent with the "disguised presentation" described by Gelinas (24) and underscores the need to identify abuse as a critical factor in a patient's history if psychotherapy is to be effective.

The limitations of this study are worthy of attention. Military samples, whether consisting of active duty or retired service personnel or civilian dependents, may be unique, thereby preventing generalization to other inpatient psychiatric settings. Although one-third of our patients were not serving on active duty, the life experiences of these patients may have varied dramatically from those of hospital inpatients generally, in spite of the fact that significant numbers of patients in civilian hospitals also have been affiliated with the armed services at some time in their lives. Other limitations include the higher proportion of men and smaller proportion of elderly patients (less than 10%) in our sample than in patients in many nonfederal institutions.

Although we achieved high interrater reliability by limiting the number of diagnosticians to two, the cost may have been systematic bias in our application of diagnostic criteria. Use of the Structured Clinical Interview for DSM-III-R (28) or a similar structured interview would have limited this potential source of bias.

Future research is needed to address the effects of combined abuse as a variable separate from physical or sexual abuse alone. In other studies, these effects are rarely appreciated and are lost in pooled data analyses. The abuse experiences of males are poorly understood, as are the possible psychiatric sequelae in men. This, too, is an area worthy of closer attention.

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Sleep Disturbances in Survivors of the Nazi Holocaust

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Objective and Method: *Sleep disturbances are commonly reported by victims of extraordinary stress and can persist for decades. This study was designed to test the hypothesis that survivors of the Nazi Holocaust would have significantly more and different sleep problems than depressed and healthy comparison subjects and that the severity of the survivors' problems would be correlated with length of time spent in a concentration camp. Forty-two survivors, 37 depressed patients, and 54 healthy subjects of about the same age, all living in the community, described their sleep patterns over the preceding month on the Pittsburgh Sleep Quality Index, a self-rating instrument that inquires about quality, latency, duration, efficiency, and disturbances of sleep, use of sleep medication, and daytime dysfunction.* Results: *The survivors had significantly greater sleep impairment than the healthy comparison subjects, as measured by all subscales of the index, but had less impairment than the depressed patients except on the sleep disturbances and daytime dysfunction subscales. However, for specific items within these subscales, survivors had significantly more frequent awakenings due to bad dreams and had less loss of enthusiasm than the depressed subjects. Sleep disturbances and frequency of nightmares were significantly and positively correlated with the duration of the survivors' internment in concentration camps.* Conclusions: *These findings suggest that for some Holocaust survivors, impaired sleep and frequent nightmares are considerable problems even 45 years after liberation.*

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Impaired sleep, "the hallmark of posttraumatic stress disorder" (PTSD) (1), is commonly reported in victims of emotional trauma; however, the specifics of this symptom remain unclear. Polysomnographic studies of elderly former prisoners of war (2), combat veterans (3–6), and torture victims (7) have used small samples and provided conflicting evidence regarding a sleep architecture particular to PTSD. Furthermore, studying victims of emotional trauma in a laboratory places additional stress on people whose "stress response system" is already hypersensitive to environmental stimuli (8). To our knowledge there are no studies reporting the pattern of sleep and the nature of the sleep disturbances in trauma victims assessed in their natural environment.

Complicating the study of the evolution of traumatic stress reactions over many years are interceding stressors and losses, concurrent substance abuse (9), and the normal changes of aging (such as altered sleep patterns) that may be mistakenly identified as posttraumatic symptoms. Studies of World War II combat veterans (10) and former prisoners of war (11) suggest that most symptoms of PTSD improve with time; however, significant symptoms, especially disturbed sleep and frequent nightmares, have been reported as much as 45 years after the stressor occurred.

Jewish survivors of the Nazi Holocaust experienced extraordinary emotional trauma. The "concentration camp syndrome" (12, 13) includes symptoms of anxiety and depression and is "invariably accompanied by insomnia and nightmares" (14). After almost 5 decades, as survivors enter their geriatric years, clinical observations disclose many residual emotional symptoms, including affective blunting (alexithymia), inability to grieve, anhedonia, and reduced tolerance of stress (15, 16). However, qualitative and quantitative aspects of sleep disturbances in a naturalistic setting have not previously been reported for these individuals.

This study assessed the sleep patterns and problems during a 1-month period of community-resident Holo-

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caust survivors in their home environments. We hypothesized that 1) compared to elderly healthy subjects, the Holocaust survivors would have significantly more sleep problems, 2) the profile of sleep difficulties would be qualitatively different for the survivor group from that of elderly depressed subjects, and 3) the severity of the survivors' sleep difficulties would be correlated with the length of time they had spent in concentration camps.

METHOD

The Pittsburgh Sleep Quality Index (17) was sent to 166 members (101 male, 65 female) of the Holocaust Center in Pittsburgh. The center maintains a mailing list of all persons identified as survivors of the Holocaust who live in the greater Pittsburgh area. Forty-two of the questionnaires were returned completed, 19 were returned uncompleted because the subjects had either died or relocated without forwarding addresses, four were returned uncompleted because the subjects had left Europe before 1939, and five were returned with either no response or angry letters stating that the respondents did not wish "to be experimented on again." The response rate of completed questionnaires was 25.3%.

The elderly healthy comparison subjects (N=54) and depressed (predominantly hospitalized) patients (N=37) had previously been recruited from the community as part of an ongoing research program on sleep, aging, and mental illness. All of the depressed patients and healthy comparison subjects were assessed with the Schedule for Affective Disorders and Schizophrenia—Lifetime Version (SADS-L) (18) and given diagnoses according to the Research Diagnostic Criteria (19). All of the depressed patients met the criteria for definite or probable current major depressive disorder. Details of the evaluation procedures to ascertain the comparison groups of healthy subjects and depressed patients have been published elsewhere (17). The demographics of the three groups are shown in table 1.

All subjects completed the Pittsburgh Sleep Quality Index, which consists of 19 self-rated questions designed to assess sleep quality during the preceding month. In addition, there are five questions rated by bed partners that are used for clinical information but are not tabulated in the final index score. The seven subscales of the index provide subjective assessment of sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances (such as nightmares), use of sleep medication, and daytime dysfunction. All components are weighted equally on scales of 0–3; the maximum score of 21 reflects the poorest quality of sleep. Extensive testing with the Pittsburgh Sleep Quality Index has demonstrated that it has internal consistency, is easy to use for patients and control subjects, is able to discriminate the sleep of control subjects from that of patients with sleep disorders and depression, and is validated by concurrent polysomnographic findings.

TABLE 1. Demographic Characteristics of Holocaust Survivors, Depressed Patients, and Healthy Comparison Subjects in a Study of Sleep Disturbances

	Sex[a]		Age (years)		
Group	M	F	Mean[b]	SD	Range
Survivors (N=42)	28	14	67.3	6.3	52–81
Depressed patients (N=37)	7	30	70.4	6.2	60–81
Healthy comparison subjects (N=54)	29	25	71.2	4.7	60–79

[a] Significant difference between groups ($\chi^2=19.1$, df=2, p=0.0001).

[b] Significant difference between groups (F=6.03, df=2, 130, p=0.003). Tukey's Honestly Significant Difference Test found pairwise differences between survivors and depressed patients and between survivors and healthy comparison subjects (p<0.05).

Following completion of the index, survivors were asked about the length of their concentration camp internment.

We used a one-way analysis of variance (ANOVA) to test for differences in age and chi-square tests for differences in gender between the Holocaust survivors and the elderly depressed and healthy comparison groups. We also conducted a one-way ANOVA to investigate the differences among the groups on the Pittsburgh Sleep Quality Index global score and the seven subscale scores. Tukey's post hoc pairwise comparison tests were also computed. Item analysis of the daytime dysfunction and sleep disturbances subscales was performed by means of chi-square tests. The groups were divided into those subjects with scores of 0 and 1 (no disturbance or mild disturbance) and those with scores of 2 and 3 (moderate to severe disturbance).

We calculated Pearson's correlation coefficients to determine the relation between the index global score and age for each of the groups, and a series of t tests was performed to investigate gender differences in the global scores and the subscale scores for each of the groups.

The distribution of global scores for the survivors was examined with chi-square tests. The subjects were categorized as those with sleep in the normal range (global scores of 5 or less), those with moderately impaired sleep quality (scores of 6–10), and those with severely impaired sleep (scores of 11 or more). A Pearson correlation was done to test the relationship between the number of years that survivors had spent in camps and their global index scores. We used Student's t test to compare the number of years spent in camps by survivors who awakened at least once a week because of bad dreams and those who reported less frequent nightmares.

RESULTS

The survivor group was younger than the healthy and depressed groups (see table 1); however, age was

TABLE 2. Subscale and Global Scores on the Pittsburgh Sleep Quality Index of Holocaust Survivors, Depressed Patients, and Healthy Comparison Subjects

Pittsburgh Sleep Quality Index	Score[a] Survivors (S) (N=42) Mean	 SD	 Depressed Patients (D) (N=37) Mean	 SD	 Healthy Comparison Subjects (C) (N=54) Mean	 SD	One-Way Analysis of Variance F[b]	 df[c]	Significant Post Hoc Pairwise Comparisons[d]
Subscale									
Sleep quality	1.29	1.04	2.03	0.86	0.22	0.42	59.11	2, 128	SD, SC, DC
Sleep latency	1.26	1.04	1.94	1.11	0.45	0.61	29.05	2, 124	SD, SC, DC
Sleep duration	1.00	0.95	2.06	1.06	0.44	0.69	35.46	2, 127	SD, SC, DC
Sleep efficiency	1.43	1.28	2.18	1.11	0.19	0.63	42.59	2, 123	SD, SC, DC
Sleep disturbances	1.63	0.84	1.36	0.54	1.04	0.39	11.04	2, 126	SC, DC
Sleep medications	0.57	1.04	1.11	1.34	0.07	0.33	13.08	2, 129	SD, SC, DC
Daytime dysfunction	0.90	0.82	1.19	0.91	0.26	0.48	19.63	2, 130	SC, DC
Global	8.15	5.28	11.84	3.72	2.64	1.79	61.69	2, 117	SD, SC, DC

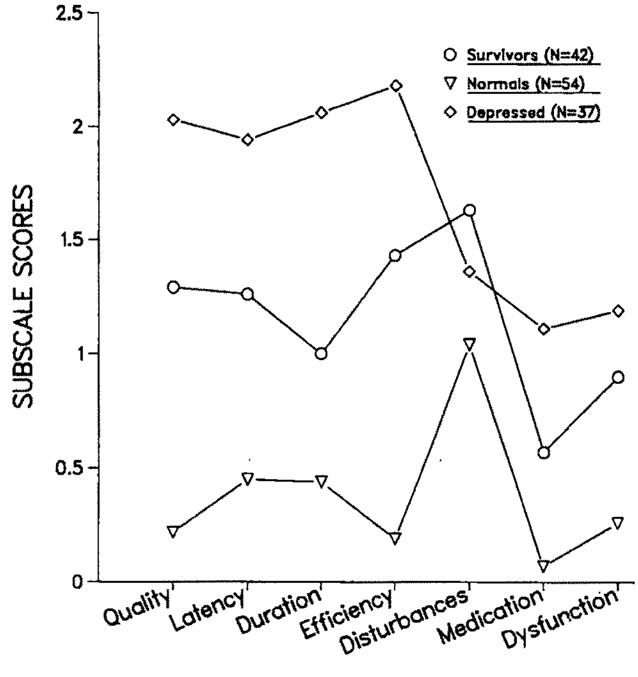
[a] Higher score indicates greater impairment.
[b] Every F ratio was significant at $p<0.0001$.
[c] Varying degrees of freedom reflect missing data on some items.
[d] $p<0.05$, Tukey's Honestly Significant Difference Test.

not correlated with total index score or any subscale score in any of the three groups (survivors: $r=0.28$, $df=37$, $p=0.18$; depressed patients: $r=0.28$, $df=29$, $p=0.13$; healthy subjects: $r=-0.03$, $df=48$, $p=0.86$). In addition, it is unlikely that the 3- or 4-year difference in age between these groups, although statistically significant, had any clinical importance. The survivor group had a higher percentage of men (67%) than the other two groups (19% and 54% for the depressed and healthy groups, respectively); however, gender had no effect on the total index score or subscale scores in any of the groups.

Of the survivors who responded, 34 had been in concentration camps and eight had been in slave labor or in hiding. All of these subjects had suffered the loss of family members and home and had endured extraordinary emotional and physical hardship. Of the 34 who had been in concentration camps, the mean±SD duration of incarceration was 2.5±1.7 years (range=0.1–5.8 years; median=2.9 years).

Total Pittsburgh Sleep Quality Index scores were available for 39 of the 42 survivors, 31 of the 37 depressed patients, and 50 of the 54 healthy comparison subjects. The lower numbers of subjects reflect isolated missing data on some items. A total index score in the normal range (5 or less) was found for 35.9% (N=14) of the survivors; 30.8% (N=12) had scores in the moderately impaired range (scores of 6–10), and 33.3% (N=13) reported severely impaired sleep (scores of 11–21). Only 3.2% (N=1) of the elderly depressed patients had scores in the unimpaired range, and 35.4% (N=11) and 61.2% (N=19) were in the moderate and severely disturbed range, respectively. Among the healthy subjects, 94% (N=47) were in the normal range and 6% (N=3) reported moderately impaired sleep; none had scores in the severely impaired range. The mean±SD total index scores were significantly different among the three groups (survivors: 8.15±5.28; healthy subjects: 3.0±2.40; depressed patients: 11.83±3.72) (see table 2).

FIGURE 1. Mean Pittsburgh Sleep Quality Index Subscale Scores of Holocaust Survivors, Depressed Patients, and Healthy Comparison Subjects (Normals)[a]



[a] All groups differed significantly on subscale scores with the exception of survivors and depressed patients on the subscales of sleep disturbance and daytime dysfunction.

On all seven index subscales, the survivors reported significantly more sleep difficulties than did the healthy comparison subjects (see figure 1). With the exception of the subscales for sleep disturbances and daytime dysfunction, the depressed group had significantly higher total index and subscale scores than the survivor group.

Although the subscale scores for sleep disturbances and daytime dysfunction did not differ between the depressed and survivor groups, specific individual items within those subscales were different between the two groups. In particular, the Holocaust survivors had significantly more awakenings due to complaints of "bad dreams," "cannot breathe comfortably," and "other" ($\chi^2=4.11$, df=1, $p<0.04$; $\chi^2=4.36$, df=1, $p<0.04$; and $\chi^2=5.45$, df=1, $p<0.02$, respectively). "Other" included hot flashes, bad memories, and nervousness. Awakenings due to needing to use the bathroom, coughing or snoring, feeling too hot or cold, or pain did not differ between the two groups.

Similarly, within the subscale for daytime dysfunction, the item "keeping up enthusiasm to get things done" was reported as a moderate or severe problem for 31% (N=13) of the survivors, compared to 62% (N=23) of the elderly depressed patients ($\chi^2=7.72$, df=1, $p<0.005$). Daytime drowsiness did not differ between the two groups.

There was a significant correlation between number of years in a camp and total score on the Pittsburgh Sleep Quality Index (Pearson $r=0.39$, df=39, $p<0.01$; Spearman rank-order correlation, $r_s=44$, df=37, $p<0.005$). The survivors who experienced awakenings due to bad dreams at least once a week (36%, N=15) had been incarcerated for a longer period of time than the group who had less frequent nightmares (mean±SD=2.8±1.7 years versus 1.4±1.7 years; $t=-2.70$, df=39, $p<0.01$). The strength of this relation was not affected by partialing out age or gender.

DISCUSSION

Sleep disturbances were found to be significant problems for approximately two-thirds of this sample of Holocaust survivors 45 years after the end of World War II. Although the comparison groups were not exactly matched for age, all groups were in the same age range, and neither age nor gender was correlated with total or subscale scores on the Pittsburgh Sleep Quality Index within any group.

The severity and profile of sleep problems were distinct for the survivor group compared to the elderly depressed and healthy comparison subjects. The survivor group scored significantly higher than the healthy subjects on the total index score and all subscales and lower than the depressed patients on the total index score and all but two subscales, sleep disturbances and daytime dysfunction. On these particular subscales, individual item differences highlighted important distinctions between the two groups. Specifically, survivors reported significantly more disturbed sleep due to bad dreams but less loss of enthusiasm during the day than did the depressed group.

Global score on the Pittsburgh Sleep Quality Index was correlated with number of years in a concentration camp. Furthermore, the group of survivors who had frequent nightmares had spent more time in camps. Taking into consideration the severity of the emotional trauma the survivors had experienced during the war because of factors other than incarceration, as well as life events and stressors since the end of the war, the strength of this relationship (even though modest) after almost 5 decades is remarkable. These correlations suggest that the duration of a stressor may have important implications for residual sleep disturbances even decades later. An alternative explanation is that the survivors who had spent a longer time in concentration camps were likely to have been exposed to more severe trauma (e.g., physical torture or a greater degree of malnutrition), which resulted in more intensive and enduring trauma-related symptoms, such as sleep disturbance. Further studies exploring the prognostic implications of extraordinary stress of long and short duration are needed.

In this study, age was not correlated with Pittsburgh Sleep Quality Index scores or frequency of nightmares. Because the subjects' current ages would correlate reasonably well with their ages at the time of trauma (since for all survivors the massive traumatic stress ended in 1945), it is reasonable to conclude that these data do not suggest that age at the time of trauma is a critical factor in determining long-term prognosis. However, most of our respondents were adolescents or young adults at the time of liberation. Further studies comparing survivors who were children, adolescents, and adults at the time of liberation are necessary to determine the effect of age on the long-term prognosis.

Although 21% of the survivors reported their quality of sleep as very bad, only 9% reported severe difficulty with keeping up enthusiasm to get things done, suggesting that sleep disturbance and impaired functioning were not necessarily linked in all members of this sample. There is evidence of a greater prevalence of anxiety and depression in Holocaust survivors (12, 13) and former World War II prisoners of war (8, 20, 21). Furthermore, Kaminer and Lavie (22) reported that Holocaust survivors with good adjustment had significantly less dream recall during REM sleep than did poorly adjusted survivors and control subjects, with control subjects having the highest dream recall of the three groups. The relationship of sleep to social functioning or specific psychiatric diagnoses was not specifically assessed in our study.

In conclusion, this study demonstrated that for many survivors of the Nazi Holocaust, impaired sleep remained a problem 45 years after the war ended. The Pittsburgh Sleep Quality Index sleep profile was different for the survivor group than for the groups of elderly healthy subjects and depressed patients. Furthermore, the severity of sleep disturbance and frequency of nightmares were related to the duration of internment in a concentration camp. Further studies of elderly victims of trauma that examine the relation of sleep (in a natural setting) to social and emotional functioning are needed to learn more about the long-term effects of extraordinary stress.

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Cognitive Deficits and Psychopathology Among Former Prisoners of War and Combat Veterans of the Korean Conflict

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Objective: This study was conducted to describe the long-term psychological and psychiatric sequelae of prisoner of war (POW) confinement against the backdrop of psychiatric evaluations of Korean conflict repatriates more than 35 years ago. *Method:* A group of 22 POWs and a group of 22 combat veteran survivors of the Korean conflict were compared on measures of problem solving, personality characteristics, mood states, and psychiatric clinical diagnoses by means of a battery of psychometric instruments and structured clinical interviews. *Results:* Although the two groups were similar in background and personal characteristics, they differed in reports of life adjustment problems, complaints of physical distress, proficiency on cognitive tests, objectively measured personality characteristics, and assigned psychiatric diagnoses. *Conclusions:* Illustrated by a case report which describes the prolonged brutality of the Korean conflict POW experience for one individual, the results suggest that the psychiatric symptoms documented more than three decades ago have persisted in severity and chronicity. In addition to problems with cognitive deficits and complaints of bodily discomfort, most common among POW survivors were symptoms of suspiciousness, apprehension, confusion, isolation, detachment, and hostility.

(Am J Psychiatry 1991; 148:67–72)

American servicemen taken captive during the Korean conflict were subjected to extraordinary stress. Of more than 7,100 war prisoners, approximately 40% did not survive captivity, and one in four has died since release (1). Capricious killings, forced marches, camp relocations, sustained nutritional deprivation, threats of death and nonrepatriation, confinement in shackles, solitary confinement, brutal tortures, and widespread disease were common occurrences for prisoners of war (POWs). These captured U.S. servicemen were also the first to be subjected to a program of mass indoctrination, which included group and individual interrogations, incessant demands for self-criticism and compliance, and structured reeducation sessions. Described by Hinkle and Wolff (2), Chinese indoctrination incorporated such tactics as isolation of resistance leaders, strategic placement of captive informants among prisoner groups, and group persuasion combined with physical privation, harsh punishments, and physical isolation to render prisoners susceptible to ideological persuasion.

Despite these unique aspects, since the initial psychiatric interest there have been few efforts to describe the residual emotional and behavioral effects of captivity during the Korean conflict. Summarizing the findings of psychiatric interviews and psychological test protocols given to newly released American POWs, Segal (3) and Strassman et al. (4) called attention to apathy toward environmental stimuli, apprehensiveness, suspiciousness, confusion, perturbation, and underlying guilt and hostility as paramount among the former prisoners' psychological symptoms. These researchers pointed to isolation from others, noncommital posture, suppressed feelings, prominent dependency needs, and low mood tone as characteristic of the newly liberated captives. Some years later, Keehn (5) commented that former POWs from the Korean conflict showed more exaggerated feelings of frustration and anger than combat veterans of the same military action and were more inclined to impatient, impulsive acts.

Recently, we described the Korean conflict POW experience and its long-term psychosocial sequelae in a small sample of survivors (6). Results of that study showed that, frequently, American forces were out-

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numbered and surrounded in combat, with massive casualties exacted before survivors were seized. Over half the men reported exposure to extreme temperatures, forced marches, diseases of malnutrition, parasites, worm infestations, severe weight loss, intimidation by psychological abuse, physical torture, and solitary confinement. More than 35 years after the trauma of confinement, their clinical picture reflected concerns about deterioration in health and physical disabilities, weaknesses on standardized measures of attention, concentration, and memory, and remarkable homogeneity in expression of psychiatric disorders. Posttraumatic stress disorder (PTSD) was identified in 90%–100% of the cases, and 85% of the men were assigned additional psychiatric diagnoses, predominantly mood and other anxiety disorders.

Complementing early descriptions of survivor psychopathology, these results supported the view that psychiatric disorders—primarily PTSD complicated by other anxiety and mood symptoms—develop predictably under conditions of extreme, prolonged stress and fail to abate with time. Additional work is required to test this hypothesis, and comparisons of POW survivors with appropriate samples of combat veterans who have seen similar military duty are essential to assess the relation between the trauma of POW confinement and the expression of PTSD and coexisting mental disorders. We conducted these comparisons using measures of problem-solving functions, personality characteristics, mood states, and psychiatric clinical diagnoses.

METHOD

The participants were 22 Korean conflict POW survivors and 22 veterans who had seen similar combat but had not been taken captive. The former POWs had responded to the Veterans Administration (VA) invitation mandated by Public Law 97-37 to undergo medical evaluation, and they completed the psychiatric and psychological assessment portions of our study protocol as well. These 22 were all of the Korean conflict POW survivors seen over a 3-year period at our VA medical center and represented more than one-half of the former POWs in our catchment area. The combat veterans were recruited by letters describing psychological and psychiatric assessment studies sent to veterans selected randomly from among patients listed on VA medical center records and commanders of American Legion and Veterans of Foreign Wars posts.

The former POWs and combat veterans did not differ significantly in race (68% and 86%, respectively, were white), age (mean±SD=56.32±4.00 and 58.41±5.14 years, respectively), education (mean±SD=10.18±3.14 and 11.50±3.29 years, respectively), socioeconomic status according to the Hollingshead-Redlich criteria (7) (64% and 77%, respectively, were middle or lower middle class), military rank (68% of both groups were noncommissioned officers), marital status (86% and 68%, respectively, were married), or employment status (55% and 59%, respectively, were employed or voluntarily retired; 23% and 27% were medically disabled). The former POWs had been captured at a young age (mean±SD=21.14±2.77 years) after serving 4.77±3.80 months in combat, had been interned for 28.05±11.20 months, and had sustained marked weight loss during confinement (35.77%±11.77% of their precapture weight). The combat veterans had entered the war zone at a similar age (20.95±5.68 years) and reported more combat exposure (14.14±6.61 months) than the former POWs ($F=33.19$, $df=1, 42$, $p<0.01$).

The assessment protocol included a structured clinical interview conducted by an experienced psychiatrist or psychologist that had items describing premilitary background and adjustment, childhood and adolescent emotional or behavioral problems, combat and POW confinement experiences, work and family history subsequent to duty in Korea, lifetime alcohol and drug use patterns, psychological problems, and physical complaints. The battery of psychological instruments included the WAIS-R, the logical memory subtest of the Wechsler Memory Scale (8) scored according to Russell's procedure (9), the MMPI, the Beck Depression Inventory (10), the State-Trait Anxiety Inventory (11), and an adjustment problem checklist modeled after one used by Foy et al. (12).

DSM-III psychiatric diagnoses for current mental disorders except PTSD were generated in individually supervised sessions where participants were administered the computerized version (13) of the National Institute of Mental Health Diagnostic Interview Schedule (DIS) (14), a structured interview used successfully by other research teams to identify psychiatric disorders among samples of traumatized subjects (15, 16). Symptoms of PTSD were evaluated by a psychologist who administered the PTSD portion of the DIS structured interview together with a *DSM-III-R*-derived checklist.

Data analysis involved chi-square tests for categorical variables and one-way multivariate analyses of variance for continuous variables. We used a Bonferroni procedure to examine univariate tests for significance and to protect against type I error because of the large number of comparisons. The usual alpha level (0.05) was divided by the number of variables ($N=62$), which meant that a p value <0.0008 was required for statistical significance.

RESULTS

The POW survivor and combat groups were similar in background characteristics, and there had been few instances of emotional or behavioral problems during the developmental years. More than half (55%) of the 44 men had been raised by their biological parents in intact homes with adequate financial support. Men who came from rural childhood environments and those from urban environments were evenly distrib-

TABLE 1. Experiences of 22 Prisoners of War During the Korean Conflict

Experience	N	%
Exposure to temperature extremes	18	82
Forced marches	16	73
Intimidation	16	73
Confinement illnesses	16	73
Weight loss>35%	15	68
Beatings	15	68
Personal death threats	14	64
Overcrowding	14	64
Interrogations	14	64
Solitary confinement	14	64
Being wounded at capture	13	59
Physical torture	13	59
Brainwashing/reeducation	13	59
General death threats	12	55
Witnessing others being tortured	11	50
Being fired on by Allies	6	27

TABLE 2. Selected Adjustment Problem Checklist Endorsements of Former Prisoners of War and Combat Veterans of the Korean Conflict

	Former Prisoners of War (N=22)		Combat Veterans (N=22)		χ^2
Problem	N	%	N	%	(df=1)
Difficulty with memory	22	100	14	64	9.78
Difficulty concentrating	20	91	7	32	16.20[a]
Tension and anxiety	20	91	12	55	7.33
Irritability	19	86	9	41	9.82
Depression	19	86	9	41	9.82
Restlessness	19	86	9	41	9.82
Feeling emotionally numb	18	82	6	27	13.20[a]
Trouble trusting others	18	82	10	45	6.29
Inability to express feelings	17	77	5	23	13.09[a]
Loss of interest in usual activities	17	77	5	23	13.09[a]
Vivid memories of unpleasant events	15	68	9	41	3.30
Marked self-consciousness	14	64	7	32	4.46
Excessive jumpiness	13	59	4	18	7.77
Nightmares	13	59	7	32	3.30
Pervasive disgust	13	59	5	23	6.02
Difficulty obtaining employment	13	59	8	36	2.28
Avoidance of activities suggesting unpleasant experiences	12	55	7	32	2.32
Lack of leisure activities	10	45	8	36	0.38
Difficulty maintaining employment	9	41	1	5	8.28
Hostility/violence	7	32	3	14	2.07
Suicidal thoughts	6	27	2	9	2.44
Problems with authority	5	23	2	9	1.53
Panic attack	5	23	3	14	0.61

[a] p<0.0008 (Bonferroni-adjusted significance level).

uted between the groups. Approximately four of every five men in both groups had dropped out of school before high school graduation, and 14% cited histories of school suspensions and/or expulsions. Truancy (18%) and juvenile arrests (9%) were reported with low frequency. None of the sample described alcohol abuse, adult arrests, psychiatric care, or suicide attempts before entering the service.

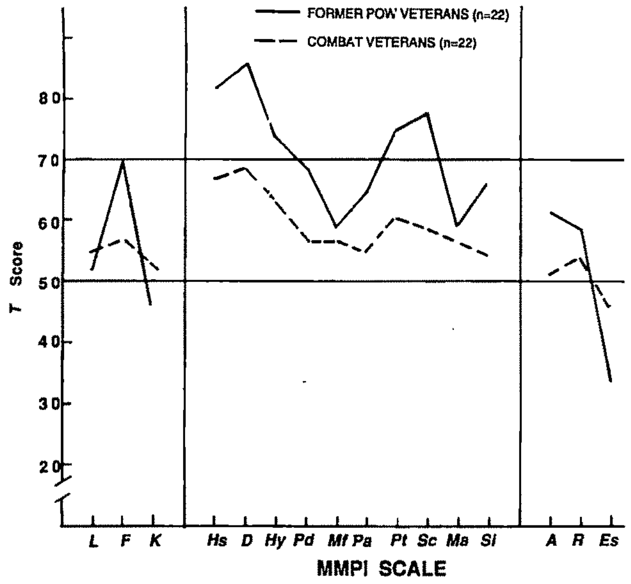
The former POWs reported involvement in fierce combat with heavy casualties before capture by North Korean/Chinese armies. During internment, they endured brutal and degrading conditions, including exposure to senseless and seemingly random prisoner executions, severe beatings and physical torture, formal programs of indoctrination and reeducation, constant death threats, prolonged semistarvation and resulting malnutrition, exposure to temperature extremes, overcrowded and unsanitary conditions, and high death rates. Some of the more common confinement stressors, derived from the POW Trauma Index (17), are outlined in table 1.

The 22 POW survivors described greater problems in adjustment and daily functioning, encompassing physical, emotional, and behavioral domains, than did the 22 combat veterans. Chi-square comparisons showed significantly higher prevalences of gastrointestinal symptoms (86% versus 32%) and severe headaches (68% versus 14%) among the former POWs than among the combat veterans. Also notable, but failing to exceed the conservative criterion for significance, were the greater prevalences of respiratory disorders (68% versus 23%), dizziness and/or fainting spells (55% versus 18%), easy fatigability (73% versus 41%), problems related to sexual functioning (55% versus 23%), and loss of weight or appetite (36% versus 9%) among the former POWs.

As shown in table 2, the groups differed significantly in their reports of problems with concentration, emotional numbing, inability to express feelings, and loss of interest in usual activities. In addition, problems with memory, tension and anxiety, irritability, depression, restlessness, and interpersonal distrust were cited by more than 80% of the POW sample. More than half of both groups admitted discrete periods of excessive alcohol consumption.

The former POWs performed more poorly than the combat veterans on the WAIS-R problem-solving measures (F=2.19, df=14, 29, p<0.05). However, differences between groups did not achieve significance under the Bonferroni procedure on the full scale (91.64± 9.57 versus 101.18±13.91), verbal (93.36±10.24 versus 101.09±14.26), and performance (90.09±9.92 versus 100.91±12.27) summary scores. A significant difference was observed on the digit span subtest score (7.55±1.97 versus 10.50±2.84; F=16.07, df=1, 42, p<0.0008). The POW survivors performed less proficiently than the combat veterans on the Wechsler Memory Scale indices overall (multivariate F=10.41, df=2, 41, p<0.01); the former POWs had significantly poorer scores on the immediate memory index (3.14±

FIGURE 1. Mean MMPI Profile Patterns of Former Prisoners of War and Combat Veterans of the Korean Conflict



1.16 versus 1.58±1.15 [higher score indicates poorer performance]; F=19.88, df=1, 42, p<0.0008). Although they also performed with less sophistication on tests of delayed memory (2.60±1.00 versus 1.61±1.33), this difference was not significant (F=7.78, df=1, 42). Russell's criteria (9) for classifying memory performances categorized 36% and 77% of the 22 former POWs as impaired on immediate and delayed recall measures, respectively, compared to 41% and 32% of the 22 combat veterans.

Dramatic between-group differences were found for MMPI descriptions of personality characteristics and psychopathology (F=2.94, df=22, 21, p<0.01; see figure 1). The POW survivors produced significantly more elevated profile configurations and scored significantly higher (df=1, 42, p<0.0008) than combat veterans on MMPI scales F (infrequency) (F=20.17), D (depression) (F=19.69), Sc (schizophrenia) (F=16.96), and Si (social introversion) (F=13.10) and significantly lower on the Es (ego strength) scale (F=14.05). They also scored significantly higher on the Keane et al. (18) PTSD scale (23.64±9.70 versus 11.45±6.32 (F=24.36). The former POWs' scores on the Beck Depression Inventory (18.27±9.36) and the anxiety state (48.00±13.73) and anxiety trait (49.09±12.17) measures, though higher than those of the combat veterans (Beck inventory, 9.05±8.08; anxiety state, 48.00±13.73; anxiety trait, 36.54±11.93), did not exceed the criterion for statistical significance.

Remarkable differences were found between the two groups of veterans in DIS-generated diagnoses based on symptoms within the past month. Mental disorders were organized into diagnosis/no diagnosis categories and into PTSD and other anxiety disorder, mood disorder, and alcohol abuse subsets. As many as 86% of the former POWs were assigned at least one diagnosis, compared to 18% of their combat-only counterparts. The former POWs showed significantly higher prevalences of anxiety disorders in general and PTSD specifically than did the combat veterans. PTSD or other anxiety disorder was identified in 86% of the former POWs, compared to 14% of the combat veterans (z=7.20, p<0.0008); 86% of the POW and 9% of the combat veterans met the criteria for a PTSD diagnosis (z=7.70, p<0.0008). Mood disorders were identified in 32% of the former POWs and 5% of the combat veterans, but the groups did not differ significantly in assignments of this diagnostic classification (z=2.45). No veterans were assigned alcohol abuse diagnoses. With few exceptions, diagnoses of PTSD in the POW survivors were associated with coexisting mental disorders, i.e., other anxiety disorders in 55% and affective disorders in 32% of the cases. No concurrent diagnoses were recorded among the combat veterans.

CASE REPORT

The following case history documents one serviceman's Korean conflict POW experience and highlights the more salient residual psychological effects.

Mr. A, the oldest of six children, was a 59-year-old veteran. At age 17 he had enlisted as an Army medic; he served from 1947 to 1949, and when he reenlisted he was assigned to duty in Korea. He saw combat for only a few days before his outfit was overrun by the North Koreans. American forces were grossly outnumbered, and retreat was announced. While attempting to evacuate the wounded, Mr. A was captured. He was held prisoner by the North Koreans for 18 months and by the Chinese for another 20 months.

Mr. A refused to cooperate with his captors. He declined to attend classes, study Communist reading materials, and sing songs praising Mao Tse-tung. He refused to offer information and to write or sign confessions. His efforts to care for the wounded and procure food for himself and others were punished as criminal infractions by his captors. He was beaten repeatedly, hung by his thumbs and arms, made to balance with his knees positioned on a stick under armed guard, imprisoned in boxes above and beneath the ground, tortured by other means, tried and sentenced to death, subjected to mock executions, and exposed to extreme temperatures without protection. Labeled "reactionary" and "incorrigible," he was cast into a hole where he was confined in isolation for more than 16 months. The cover of his hole was opened perhaps once a day, when his captors dropped down small amounts of food which he shared with vermin. Occasionally, his solitary confinement was broken by interrogations or forced work details. His weight dropped to 80 lb, or 55% of his preconfinement weight. He suffered frostbite of his fingers and toes, coughing episodes with hemoptysis, and profuse rectal bleeding.

On his return to the United States, Mr. A was found to have paragonimiasis of the lungs and intestinal amebiasis. He was hospitalized for several months, treated for his lung condition, and awarded 10% disability. He indicated that he had never been questioned about the psychiatric effects of his experiences. Having been uninterested in talking in general, he had not volunteered information. He said that he had found most health care professionals disinclined to listen and uninterested in his physical problems. He suffered sleep disturbances, nightmares, extreme fear of the Communists, marked interpersonal suspicion, claustrophobia, severe depression, and heightened anxiety. He reported longstanding headaches, sensations of knots in his chest, difficulties in swallowing, and aches throughout his body. Behavioral observations suggested that he was absorbed in vivid memories of unpleasant experiences, likely to lose track of purposeful activity, emotionally labile and volatile (particularly when recounting captivity experiences), and easily angered.

Mr. A has been involved in psychotherapy for approximately 3 years. During his first session, he inquired if he would be "interrogated," but he appeared to be eager to have someone listen to and understand his experiences. Since he must travel some distance to keep appointments, a novel approach was taken. Sessions have been scheduled every 2–3 weeks for 3 hours each, allowing sufficient time for abreaction and mastery of composure within the safety of the therapeutic relationship. Mr. A has never been late or missed a session. Continuity of process has not been disturbed because of his high investment in altering his response to stress and achieving symptomatic relief.

DISCUSSION

Although our sample of American servicemen were among the 60% who survived imprisonment, our data suggest that their endurance was accomplished at a great personal price. Their impairments in cognitive, emotional, behavioral, and interpersonal functioning were remarkably severe and persistent in comparison with the impairments of the other combat veterans.

Clinical and research reports have pointed out that problems with memory, concentration, and learning are common among POW survivors. Goldstein et al. (19) found that 62% of World War II former Japanese-held POWs complained of memory and concentration impairments, and Sutker et al. (20) reported that 78% and 93% of two World War II and Korean conflict POW subgroups cited similar problems. In the present study, POW survivors were deficient relative to combat veterans of similar ages and educational characteristics on the WAIS-R and Wechsler Memory Scale tests of cognitive performance, showing significantly poorer performance on tasks that require attention, concentration, and memory. An association between cognitive impairment and severity of biological and psychological stress reflected by weight loss during captivity was reported by Sutker et al. (21) among World War II and Korean conflict POW survivors, and European researchers have described a possible link between organic brain changes and intellectual impairment among Danish and Norwegian survivors of Nazi concentration camps (22, 23).

The picture of psychopathology among the POW survivors is presented vividly by the MMPI and psychiatric interview data. Their MMPI profile configurations differed dramatically in elevation and shape from those of the combat veterans, with evidence of clinical depression, somatic preoccupations, interpersonal detachment, social alienation, negative ruminations, and self-devaluation. These symptoms are compatible with the DIS-generated clinical diagnoses of the former POWs, 86% of whom were considered to be suffering from PTSD. Not surprisingly, two of the 22 combat veterans were also assigned PTSD diagnoses. The PTSD prevalence figures for the severely traumatized POW sample are higher than the 67% figure reported by Kluznik et al. (24) for predominantly German-held former POWs and the 50% estimates cited for Japanese-held POWs (19) and Southeast Asian refugees (16). It is not clear whether the higher prevalence of PTSD in our sample may be attributed to the greater severity of physical and psychological stressors endured as part of the Korean conflict POW experience or whether discrepancies in assessment procedures and diagnostic criteria, as well as other factors, contributed to the differential findings of symptoms of stress-related disorder. In any case, the high association of PTSD and other mental disorders has been reported by Mollica et al. (16) among Southeast Asian refugees and Sierles et al. (25) in Vietnam combat veterans.

Psychiatric symptoms documented more than 30 years ago among recently liberated POW survivors of the Korean conflict have persisted over time. Data generated through self-reports, personality testing, and structured psychiatric interviews complement the clinical picture provided in the mid-1950s (3, 4). Symptoms of suspiciousness, apprehension, confusion, isolation and detachment from others, guilt, and hostility remain evident, although the present results highlight marked psychological discomfort, moderate to severe dysphoria, and concerns about physical limitations and fatigue as an integral part of the psychological constellation. Evidence from this study underscores the persistence of interpersonal detachment, difficulties in expression of feelings, and inner conflict regarding disclosure versus guardedness as chronic residual effects of the psychological and biological brutalization that constituted the POW experience during the Korean conflict. The findings of cognitive deficits and bodily discomfort are of interest, and the results suggest that intense, prolonged stress may lead to development of psychiatric disorders in almost anyone, relatively independent of premorbid adjustment and/or individual difference factors, and that these are remarkably resistant to extinction over time.

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Effects of Buspirone and Alprazolam on the Cognitive Performance of Normal Elderly Subjects

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Objective: To increase understanding of the potential in elderly persons for disability related to behavioral side effects of anxiolytic medications, cognitive and psychomotor effects of clinical doses of buspirone and a popular intermediate-acting benzodiazepine, alprazolam, were examined in carefully screened, healthy elderly subjects. Method: Sixty subjects recruited through community organizations and newspaper advertisements and screened on the basis of history, physical examination, and laboratory studies were randomly assigned to one of three drug treatment groups. After 2 days of washout placebo, subjects were given 0.25 mg t.i.d. of alprazolam, 5 mg t.i.d. of buspirone, or placebo three times a day for a total of 14 days in a double-blind design. Behavioral assessments were completed beginning 1 hour after ingestion of medication on the second washout placebo day, day 1 of the treatment period, and day 14 of the treatment period. Tests included the continuous performance test, recall memory for word lists, digit-symbol substitution, retention of pictorial stimuli over 1 hour, the Profile of Mood States, and subjective ratings of mental status. Results: Buspirone did not affect reaction time, vigilance, psychomotor speed, or memory function. Alprazolam had minimal effects on vigilance, psychomotor speed, and memory on the first treatment day and had no effects after repeated doses. Conclusions: Buspirone did not produce behavioral side effects that could lead to disability, and alprazolam had minimal side effects. Because the patients were carefully screened, it is unclear whether these medications in the doses used would have more side effects in less healthy elderly patients.

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Benzodiazepines have emerged as the mainstay of pharmacologic management of anxiety disorders in the United States, but they can produce behavioral side effects. Variable impairments in reaction time (1–4) and in attentional capacity as assessed by vigilance, divided attention, and continuous performance tasks (5, 6) have been reported. Recent studies have confirmed earlier findings (7–9) that psychomotor speed and memory/learning are among the functions most sensitive to benzodiazepines. Psychomotor tasks affected by benzodiazepines include visual tracking, digit-symbol substitution, card sorting, simulated driving, and maze performance (1–6, 10–12). Smiley (13) concluded that the commonly prescribed tranquilizers diazepam and lorazepam clearly impair many aspects of psychomotor performance. Anterograde amnesia is perhaps the most troubling side effect of these medications (4, 14–23). The ability to learn new material may be impaired for at least 8 hours after ingestion of longer-acting benzodiazepines such as flurazepam (15). Delayed recall may be impaired for word lists learned more than 8 hours after ingestion of the shorter-acting triazolam (23). Although little is known about the nature of memory impairment, the fact that retention is normal for material learned before drug administration (4, 16–18, 21–24) suggests that retrieval processes may be relatively spared. The ability to learn skills or procedures may also be spared (17).

Behavioral side effects are frequently reported for lorazepam, diazepam, flurazepam, and triazolam, but the potential for side effects appears to be lower for some other benzodiazepines. Negative findings have been reported for chlordiazepoxide, prazepam, and chlorazepate on tests of their effects on psychomotor speed and reaction time (25, 26). Bond et al. (10) re-

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ported no effects on reaction time, arithmetic, and psychomotor tasks in anxious patients treated with chlordiazepoxide and they reported only minimal effects for medazepam and diazepam. The amnestic effects of lorazepam and triazolam have been contrasted to the negative findings for chlorazepate (22) and temazepam (23).

Unlike benzodiazepines, buspirone, a serotonin agonist, has been reported to have no effect on psychomotor abilities (e.g., tracking, simulated driving, and digit-symbol substitution tasks) or attentional capacity (divided attention tasks) (2, 3, 6, 11, 27, 28). Short-lasting effects on vigilance during the absorption phase of the drug are milder than those of benzodiazepines (5). The minimal effects on vigilance and reaction time reported with buspirone tend to occur when the medication is administered in a single dose in the range of 20 mg and to subside within 3–5 hours (5, 27). Although buspirone has little effect on vigilance and psychomotor skills, the potential effects on memory function remain unknown.

The relative effects of buspirone and benzodiazepines have not been systematically evaluated in the elderly. Prescribing anxiolytics for elderly patients is complicated by the potential for disability related to behavioral side effects. To understand this potential for disability, we investigated the cognitive and psychomotor effects of buspirone and a popular intermediate-acting benzodiazepine, alprazolam, in normal elderly subjects.

METHOD

The sample consisted of 60 subjects, at least 62 years of age, recruited from community organizations and newspaper advertisements. Medical histories, physical examinations, psychiatric interviews, and laboratory studies were used to rule out clinically significant and/or uncontrolled systemic medical illness, neurologic disease, psychiatric disorders, persistent insomnia, and histories of substance abuse. Persons taking β blockers, clonidine, methyldopa, benzodiazepines, monoamine oxidase inhibitors, antihistamines, or sedative hypnotics were excluded. The subjects were randomly assigned to one of three drug treatment groups that were similar in age, education, race, and sex composition (except for a lower percentage of women in the buspirone group) (see table 1).

The mean±SD score for all subjects on the General Health Questionnaire (30) was 11.92±3.34, and the mean±SD T score on the Global Severity Index from the Hopkins Symptom Checklist (31) was 46.35±8.16), indicating the absence of psychiatric symptoms. There were no group differences on these measures. Test procedures were completed after the subjects gave informed consent.

TABLE 1. Characteristics and IQs of Normal Elderly Subjects Given Cognitive Tests After Ingestion of Placebo, Buspirone, or Alprazolam

Item	Placebo Group (N=20)	Buspirone Group (N=20)	Alprazolam Group (N=20)
Age (years)			
Mean	69.4	68.5	69.4
SD	5.2	4.6	4.4
Female sex			
N	13	8	13
%	65	40	65
White race			
N	19	20	18
%	95	100	90
Education			
<12 years			
N	1	1	4
%	5	5	20
12 years			
N	5	7	5
%	25	35	25
12–16 years			
N	7	6	7
%	35	30	35
>16 years			
N	7	6	4
%	35	30	20
WAIS-R (short form) (reference 29)			
Verbal IQ			
Mean	116.6	113.5	107.1[a]
SD	16.9	12.9	13.4
Performance IQ			
Mean	107.8	106.5	104.3[a]
SD	11.5	12.3	10.1
Full scale IQ			
Mean	114.4	111.4	106.7[a]
SD	14.9	12.5	12.3

[a] N=19.

Measures

Continuous performance test (32). This test was used to assess vigilance and reaction time. Enlarged letters were presented by means of an Apple IIe computer at the rate of one letter every 1.1 second (a 200-msec display followed by a 900-msec response interval). The subject was required to press a button whenever he or she saw the letter *A* followed by the letter *X* on each of 1,000 trials. The percentage of critical events was 7%.

Free recall of clustered and unclustered word lists. Word list recall was used to assess memory for verbal material requiring different levels of effort to encode. A series of 18-item lists containing six words from each of three distinct semantic categories (33) was constructed in a manner similar to that of a previously reported study (34). Each alternate form consisted of one clustered and one unclustered word list. For clustered word lists, semantically related words (e.g., tools) were grouped together. Lists were read aloud at a rate of 3 seconds per word, and subjects were asked to count backward for 15 seconds before recall.

Symbol-digit substitution and copying tasks. These tasks were used to assess psychomotor speed and incidental memory. The substitution task was similar to the WAIS-R digit symbol subtest but used seven symbols less likely to evoke verbal associations (35) paired with single-digit numbers. The task was administered in a manner similar to that of the WAIS-R digit symbol subtest except that the subjects were presented with rows of symbols and had to copy the digit associated with the symbol. Immediately afterward, the subjects were given a sheet of paper that had the seven symbol-digit boxes without the numbers. They were instructed to place the numbers below the appropriate symbols, as a measure of incidental recall. To assess motor speed, the subjects were given the answer sheet with the numbers rather than the symbols in the upper box and were instructed to copy the numbers in sequence.

Retention of pictorial stimuli. This test assessed memory retention with a paradigm designed to minimize differences in initial learning. The subjects were shown 64 slides of line drawings of common objects (36), one at a time for 1½ seconds per item. The slides were presented again for 1 second if a subject did not obtain a score of at least 75% correct on a criterion test made up of 16 of the original drawings and 16 distractors selected randomly. A second criterion test with 32 different drawings was administered if the slides were shown a second time. Recognition memory was examined at 10 minutes and at 1 hour with a different sample of 16 original drawings randomly presented with a different sample of 16 distractors. The stimulus and distractor items within each test were comparable on rated complexity and imagery agreement.

Profile of Mood States (POMS) (37). All of the subjects were given this well-known test.

Subjective ratings. This self-report measure had 21 behavioral dimensions (e.g., nervous-calm) rated by drawing a perpendicular line at the appropriate point along a vertical line. In addition to a global score, scores on four items pertaining to mental alertness (e.g., mentally slow-mentally quick) were used as an index.

Procedure

After receiving washout placebo three times a day for 2 days, the subjects were given 0.25 mg t.i.d. of alprazolam (daily dose=0.75 mg), 5 mg t.i.d. of buspirone (daily dose=15 mg), or placebo three times a day for a total of 14 days. Both the subjects and the investigators were blind to the medication received. The doses of alprazolam and buspirone were chosen on the basis of the manufacturers' recommended starting doses.

The continuous performance test and word list learning were administered before the washout period in order to familiarize the subjects with the test procedures. To obtain baseline scores, the continuous performance test, word lists, symbol-digit substitution test, digit copying test, POMS, and subjective ratings were administered beginning 1 hour after ingestion of the capsule on the second washout placebo day. All subjects were given the same measures beginning 1 hour after the first daily dose of buspirone, alprazolam, or placebo on day 1 of the treatment period and again on day 14 of the treatment period. The pictorial retention test was administered on day 1 and day 14 but not on the second placebo day. Alternate forms of the continuous performance test, word lists, and the symbol-digit, digit copying, and pictorial retention tests were independently randomized across test sessions. The order of administration of the clustered and unclustered word lists was also randomized across subjects.

The data from word list learning, symbol-digit substitution, digit copying, the POMS, and subjective ratings were analyzed by analysis of covariance (ANCOVA), with baseline scores as covariates and day 1 and day 14 scores as dependent variables. Because the pictorial retention test was not administered at baseline, data from that test were analyzed with analysis of variance (ANOVA). Planned contrasts were also used to assess the effects of medication (average of alprazolam and buspirone) versus placebo and to compare the effects of alprazolam versus buspirone. Reaction time data from the continuous performance test were normally distributed and were analyzed by means of an ANCOVA, but error scores were highly skewed and were analyzed by means of an ordinal logistic analysis in which baseline scores served as the covariates. In the ordinal logistic analysis, an exponential model was fitted to the cumulative error scores. Group differences were assessed by comparing a full model with group variables to a reduced model without group variables and obtaining a chi-square with 2 degrees of freedom by subtracting the reduced-model chi-square value from the full-model chi-square value.

RESULTS

There were no statistically significant group differences on ANCOVAs and ANOVAs for global test measures on day 1 and day 14. The three medication groups did not differ on total errors or mean reaction time for correct responses on the continuous performance test; digit copying time, processing speed (time for symbol-digit substitution minus time for digit copying), or incidental recall of symbol-digit items; total word recall (clustered and unclustered word lists); and percentage of pictures forgotten over the 1-hour retention interval. The summary scores from the POMS and subjective ratings did not differentiate the groups.

Although the groups did not differ in total errors on the continuous performance test, the alprazolam group tended to make more omission errors than the buspirone and placebo groups on test day 1; the chi-square test showed a marginally nonsignificant difference across the three groups ($p<0.06$). The frequency distribution of omission errors was nearly identical for the buspirone and placebo subjects and differed from that of the alprazolam subjects. Fifty-five percent of the buspirone and placebo subjects made no omission errors, compared to 30% of the alprazolam subjects. Thirty percent of the alprazolam subjects made three or more errors, compared to 10% of the buspirone subjects and 5% of the placebo subjects. Three alprazolam subjects made four, 13, and 20 errors of omission, but no buspirone or placebo subject made more than three such errors. Planned contrasts showed a tendency ($p<0.03$) for alprazolam subjects to copy the digits more slowly than buspirone subjects on day 1 (mean±SD=65.8±3.2 seconds versus 60.5±2.5 seconds) and a tendency ($p<0.05$) for subjects taking these drugs to recall fewer symbol-digit pairings than placebo subjects on day 1 (5.5±0.5 pairings for placebo subjects versus 4.8±0.5 for buspirone and 3.9±0.4 for alprazolam subjects). Planned contrasts showed no consistent pattern of findings on the POMS and subjective ratings.

DISCUSSION

The absence of effects of buspirone on psychomotor function, attention, and memory in our normal elderly subjects is consistent with the negative findings with divided doses reported in studies of younger subjects. Buspirone's anxiolytic action is delayed and is probably related to long-term changes in serotonergic system function (27, 28). Given the absence of sedative effects and the time course for clinical effects, any change in cognitive and psychomotor performance might be expected on day 14, once plasma steady state has been reached, rather than day 1. The absence of any effect provides evidence that buspirone does not contribute to excess cognitive or psychomotor disability in elderly persons.

The findings with alprazolam were essentially negative, although there was an indication of mild performance decrements on day 1. Subjects taking alprazolam made more omission errors on the continuous performance test and copied the digits more slowly than subjects taking buspirone or placebo. They also recalled fewer symbol-digit items than subjects taking placebo. Given the number of statistical analyses, these results might be spurious, although the pattern of findings is consistent with mild performance decrements on day 1 and lack of effect after repeated doses over the next 2 weeks. Performance decrements on the first treatment day on tests initiated 60 minutes after drug administration are not unexpected and are consistent with findings in an earlier study (1). Alprazolam is a high-potency benzodiazepine with relatively rapid absorption (peak plasma levels are reached in 1–2 hours) and potential sedating effects that may subside after repeated daily doses. Extrapolating these findings to geriatric clinical patients requires caution because of potential differences in general health status and the potential role of anxiety reduction in improving concentration.

The relative absence of effects of alprazolam on cognitive and psychomotor functions nevertheless requires explanation. Relatively less information is available on the potential behavioral side effects of alprazolam than of lorazepam, diazepam, flurazepam, and triazolam. Aranko et al. (1) administered 0.25 mg t.i.d. of alprazolam and 5 mg t.i.d. of diazepam and examined young adults on the first and seventh days of treatment. Alprazolam as well as diazepam affected digit-symbol substitution 2 hours after the first daily dose but not 6 hours later on the first treatment day. Neither drug affected visual tracking or choice reaction time relative to baseline performance. Neither drug affected performance on the seventh day of treatment. Kumar et al. (16) administered 0.50 mg t.i.d. of alprazolam and 1 mg t.i.d. of lorazepam to young adults and examined free verbal recall on the sixth day of treatment. Alprazolam as well as lorazepam impaired delayed but not immediate recall of word lists presented approximately 2 hours after the first daily dose. Further comparative studies are needed to assess the potential side effects of alprazolam relative to those of other benzodiazepines in elderly persons. The pharmacodynamic and pharmacokinetic properties of alprazolam have not been systematically studied in the elderly, but our behavioral data raise the possibility that in larger doses the effects of alprazolam may be more pronounced.

Another possible explanation for the relative absence of effects of alprazolam may be the sensitivity of the tests used. Kumar et al. (16) found impairments in delayed but not immediate free recall of word lists by subjects taking alprazolam. We did not assess delayed recall of word lists but found no evidence of abnormally fast forgetting of pictorial stimuli during a 1-hour delay. However, this test used pictures rather than words, a recognition rather than a recall memory paradigm, and a shorter delay and may not have been as susceptible to drug effects. Deficits in delayed but not immediate recall have been reported in several studies using different benzodiazepines (18, 21, 23), but one study (24) reported normal delayed recall following slow learning to criterion after intravenous administration of diazepam. The majority of studies have found deficits in immediate recall (4, 15, 17, 20, 22). Digit-symbol substitution and copying tasks have long been recognized as among the most sensitive to the effects of benzodiazepines (8, 9). In contrast, there is little information about the relative sensitivity of continuous performance tests. Erwin et al. (5) reported negative findings with diazepam when they used a simple continuous performance test of only 5 minutes' duration, but we are unaware of studies of benzodiazepine side effects that have used a continuous performance task similar to our own. Other vigilance tasks have been shown to be sensitive to the effects of benzodiazepines (5, 13, 24).

The focus of our study was on potential behavioral side effects associated with typical clinical doses and regimens of buspirone and alprazolam in elderly subjects. Buspirone did not produce behavioral side effects that could lead to disability, and alprazolam had minimal side effects. The effects of higher single or daily doses might be investigated in future studies. It is also unclear whether these medications given in the dosages we used would have more side effects in less healthy elderly patients. Our patients were carefully screened and did not have clinically significant or uncontrolled systemic medical illness, neurologic disease, psychiatric disorder, persistent insomnia, or histories of substance abuse, and they were free of other medications that might affect functioning. Although the careful screening of subjects might have limited the generalizability of our findings, these data are important for understanding the potential for excess disability attributable to medication.

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Cognitive and Behavioral Effects of the Coadministration of Dextroamphetamine and Haloperidol in Schizophrenia

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Objective: The authors sought to determine if an acute dose of dextroamphetamine might have positive effects on affect and cognition in schizophrenic patients maintained on a regimen of haloperidol and, if so, what variables might predict such improvements. Method: Twenty-one patients with chronic schizophrenia who were hospitalized on a research ward received a single oral dose of dextroamphetamine (0.25 mg/kg) in a double-blind, placebo-controlled, crossover study. All patients were receiving 0.4 mg/kg per day of haloperidol. Cognitive tests, motor tests, global ratings, mood ratings, and videotape ratings were used to determine the effect of the coadministration of these drugs. Ventricle-brain ratios derived from CT scans were used to predict response to the coadministration of these drugs. Results: Amphetamine improved performance on a measure of concept formation on the Wisconsin Card Sorting Test but did not result in changes in performance on tests of memory or attention. As a group, the patients were more active and performed psychomotor tests more quickly while receiving amphetamine. Six patients were judged by clinical raters to have improved in terms of affect, cooperation, and engagement with the environment. Improvement was associated with enlarged cerebral ventricles and increases in blink rate from the placebo to the active drug condition. No patient unequivocally worsened. Conclusions: These results may be consistent with the theory that coadministration of amphetamine and haloperidol produces relatively selective enhancement of cortical dopaminergic activity. However, because of the acute nature of the trial and the specialized research environment in which it was conducted, the authors do not advocate amphetamine as a routine clinical treatment of schizophrenia.

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Amphetamine is a potent catecholaminergic agonist that causes release of biogenic amines and blocks their reuptake (1). It is thought that amphetamine may cause or exacerbate psychotic symptoms, especially paranoia (2–4), in a manner consistent with the dopamine hypothesis of schizophrenia—that is, through dopaminergic overactivity in the limbic system and striatum (5).

There have been reports that amphetamine improves symptoms in some patients with schizophrenia (6, 7). Other dopamine agonists, including methylphenidate (8), L-dopa (9–11), bromocriptine (12, 13), and apomorphine (14, 15), used in chronic or acute trials, have also resulted in improvement in some patients with schizophrenia.

These data raise the question of whether the symptoms ameliorated by dopamimetics reflect pathologically reduced dopaminergic activity in areas outside the limbic system and striatum, such as the prefrontal cortex. Anhedonia, lack of drive and initiative, and restricted affect are symptoms sometimes attributed to prefrontal cortical dysfunction (16) and have been associated with decreases in the concentrations of the CSF dopamine metabolite, homovanillic acid (HVA) (17–19). Diminished prefrontal activity, as measured by regional cerebral blood flow during a cognitive activation procedure, has also been associated with lower concentrations of HVA in patients with schizophrenia (20).

If, in fact, dopaminergic function were reduced in the frontal cortex in schizophrenia, then the use of a dopamine agonist like amphetamine might prove efficacious in enhancing function in patients with the dis-

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ease. However, because amphetamine is not selective in terms of its regional activity, it would also increase dopamine release and block reuptake in subcortical dopaminergic systems, possibly exacerbating psychotic symptoms. Coadministration of amphetamine and a neuroleptic with primarily dopamine type 2 (D_2)-blocking effects, such as haloperidol (21), might prevent the psychotogenic effects of dopamimetic therapy. Since cortical dopaminergic receptors are primarily dopamine type 1 (D_1) (22), this strategy might in theory preferentially enhance cortical dopaminergic function. In order to test this hypothesis, we administered amphetamine acutely to patients who were receiving chronic treatment with haloperidol and assessed changes in affect and neuropsychological function.

METHOD

Patients and Design

Twenty-one patients with *DSM-III-R* diagnoses of undifferentiated or paranoid schizophrenia who were hospitalized on a research ward participated in this study. No patient had a diagnosable history of neurological disease or substance abuse. There were 14 men and seven women in the group. Their mean age was 32 years (range=20–54 years). Their mean duration of illness was 11 years (range=4–20 years). Thus, the subjects were relatively young and chronically ill. The patients exhibited both positive and negative schizophrenic symptoms. In the week prior to the study, the patients were given the Psychiatric Symptom Assessment Scale (23). Of their mean total score on this scale, 32% reflected negative symptoms, 46% reflected positive symptoms, and 11% reflected paranoid symptoms.

Informed consent was obtained from each patient. The study was approved by the National Institute of Mental Health Institutional Review Board.

A single dose of 0.25 mg/kg of dextroamphetamine elixir or placebo elixir was administered by mouth to each patient in random order in a double-blind crossover paradigm. The order of drug or placebo administration was known only to the pharmacist, who had chosen randomly. All patients had been receiving haloperidol treatment for a minimum of 6 weeks before the study and were receiving haloperidol throughout the study at a dose of 0.4 mg/kg daily. Mean time between active and placebo conditions was 4.1 days; the range was 3–7 days.

Measures and Determination of Response to Treatment

The Wisconsin Card Sorting Test (24), a task sensitive to prefrontal-type executive function, was administered in an automated format (25). Verbal fluency was measured by asking patients to generate words beginning with specific letters of the alphabet for 1 minute (26). Effortful recall and recognition were measured by the Selective Reminding Test (27). Attention was measured by a dynamically paced 5-minute version of the Continuous Performance Test (28). The speed and resistance to interference of information processing were assessed by the Stroop Color and Word Test (29). The Understanding Communication test of comprehension and reasoning (30) was also administered. It was split into alternate forms to minimize practice effects. Equivalent forms of the Selective Reminding Test and the test of verbal fluency were also used to minimize practice effects.

Spontaneous bodily rotation (360° turns summed over an 8-hour period) and partial rotational activity (90° turns) were measured by an ambulatory electronic rotometer (31), an instrument that monitors orientation changes around the individual's rostral caudal axis. Subjects wore the rotometer on their belts for 8 hours following administration of the elixir. Finger-tapping speed on a telegraph key in a 10-second epoch (32), trail-making (Trails B) (32), perseveration in drawing a design (33), and spontaneous eye-blinking in a 3-minute period of conversation were examined. Inhibition of competing motor responses was measured in a go/no go paradigm (34).

Global ratings were made by two investigators (L.B.B. and T.E.G.) who were blind to medication condition (as well as ventricle-brain ratio [VBR] and mood state inventory results—described later in this paper). Ratings were based on independent observations made while the patients were clinically interviewed and during neuropsychological testing of the patients. Because we believed that the effects of amphetamine were likely to be manifested in interpersonal responsivity, emotional breadth, and positive affect, each patient was rated in a global, "all-or-none" fashion as responding positively or not responding positively to amphetamine. The presence of any two of the following criteria resulted in classification as a positive responder (i.e., showed improvement), provided ratings of the other criteria in the same phase did not suggest deterioration: the patient 1) was more cooperative in completing various procedures, 2) displayed an elevation in mood—i.e., was less dysphoric or less anxious about life, 3) appeared less paranoid—e.g., was less fearful of harm, 4) exhibited activation or verbal expansiveness that was adaptive and appropriate, and 5) gave a subjective report of more coherent thinking, greater concentration, and more energy. The two raters classified patients as responders or nonresponders by consensus.

Because the behavioral changes we thought we were observing were subtle and not readily amenable to quantification by any single rating system, we attempted to validate our impressions by videotaping the last 14 patients who participated. One of us (L.B.B.) videotaped semistructured interviews conducted with patients 2–4 hours after the patient received amphetamine or placebo. The interviews lasted for about 30 minutes. Each taped interview was edited to a

5-minute representative excerpt so that a series of tapes could be rated. Staff members individually rated each pair of excerpts from each patient, judging on which occasion the patient appeared "better."

A patient was rated as improved according to videotaped interview if a significant number of observers, as determined by chi-square, assigned improvement to the amphetamine condition. These ratings were done at three meetings; the number of raters varied between 11 and 19 at the sessions. Filming, editing, and rating all were done blind; the code was not broken at the pharmacy until all these steps were completed.

Measures of mood, affect, and sense of energy and mental stability that might be sensitive to drug effects were also measured by the Profile of Mood States (POMS) (35), a self-report inventory. POMS data for the first six patients in the study were not collected.

Twenty subjects underwent CT scanning on a GE 9800 machine. VBR was calculated by planimetry as described elsewhere (36, 37). The size of the third ventricle was quantified by measuring it at its widest point under magnification times 7. Prefrontal cortical markings and general cortical markings were rated by using a 4-point scale (38). CT scanning was done within 1 year of the study.

Samples of venous blood were frozen at −20 C°. Assays for amphetamine levels in serum were performed by high performance liquid chromatography. The sensitivity of the procedure for detection of amphetamine was 10 ng/ml. Samples were available for 19 of the patients.

Procedure

One hour after the elixir was administered, patients began neuropsychological testing, which typically lasted for 1 hour. Samples of venous blood were drawn at 45 to 90 minutes after the elixir was administered. The Wisconsin Card Sorting Test and the POMS were administered 2 hours after the administration of the elixir. The videotaped interviews occurred about 2.5 to 3 hours after administration of the elixir. Blood pressure and pulse rate were recorded at the time of administration of the elixir and 1, 4, and 8 hours thereafter. The behavioral effects of amphetamine are thought to be maximal about 1–3 hours after oral administration (39, 40).

RESULTS

Qualitative and Subjective Responses to Treatment

After the blind was broken it was found that all six patients who were deemed positive responders to amphetamine by the consensus of T.E.G. and L.B.B. had received amphetamine on the day a positive response was noted. On the basis of the videotape ratings, four patients met criteria for improvement after the blind was broken. In these patients, chi-square analysis indicated that amphetamine and improvement were associated by a significant number of raters ($\chi^2>3.27$, df=1, $p<0.07$). These four patients were also among the six patients rated as improved by the consensus of T.E.G. and L.B.B. and were considered responders. Interviews with the other two patients rated as improved by T.E.G. and L.B.B. had not been taped. For the purposes of all further analyses they were also classified as responders. For 10 patients, improvement and amphetamine were not associated by a significant number of raters ($\chi^2<2.03$, df=1, $p>0.16$). The 10 patients who were rated as nonresponders by the group rating criteria were among the 15 patients rated as unimproved by the consensus of T.E.G. and L.B.B. Thus, 15 patients were classified as nonresponders. No patient was classified by either rating method as worse (i.e., they were rated as better during the placebo condition).

Equivocal untoward reactions were observed in three patients. One patient responded to a command hallucination that had been chronic. Two other patients exhibited brief periods of unusual behavior. One displayed irritability, and the other showed grooming stereotypies.

The point biserial correlation between response to amphetamine and VBR was 0.59 (p=0.007). Of the six patients who responded to the drug, all had VBRs greater than 7.0 ($\chi^2=8.3$). Of 14 patients who did not respond, 11 had VBRs less than 6.0 ($\chi^2=5.9$). Thus, 17 of 20 patients could be correctly classified in terms of response by using an arbitrary VBR cutoff of 7.0. VBR was significantly larger in the group of responders (t=3.27, df=18, p=0.004, two-tailed). The point biserial correlation between third ventricle width and response was not significant (r=−0.07, p=0.78). The point biserial correlations between prefrontal cortical markings (r=−0.14) and general cortical markings (r=0.16) and response were also not significant.

Increases in blink rate (from placebo to active medication) were significantly greater in the group of responders (t=3.01, df=17, p=0.01). Blink rate did not differ significantly between responders and nonresponders receiving placebo (t=0.08, df=17, p=0.93). In addition, the point biserial correlation between response and increase in blink rate scores was 0.60 (p=0.007).

Measures of Response to Treatment

The weighted raw scores on each of the six scales of the POMS (anger-hostility, vigor, confusion, fatigue, tension-anxiety, and depression-dejection) were analyzed. The responders differed significantly from the nonresponders in POMS change scores in tension-anxiety and depression-dejection. All change scores in the responding group were in the direction of improvement. These results are listed in table 1. Amphetamine did not have a significant effect on any POMS scale for the group as a whole ($t<0.90$, df=14, $p>0.38$).

TABLE 1. Change Scores on Profile of Mood States Scales for 15 Schizophrenic Patients Who Did or Did Not Respond to Amphetamine

Scale	Responders (N=4) Mean	SD	Nonresponders (N=11) Mean	SD	t (df=13)	p
Tension-anxiety	−5.5	3.4	0.9	5.8	2.06	0.06
Depression-dejection	−3.8	3.4	4.8	11.9	2.16	0.05
Anger-hostility	−4.0	3.9	1.5	9.1	1.16	0.27
Vigor	4.8	7.1	0.1	6.8	1.16	0.27
Fatigue	−5.5	9.7	1.5	6.9	1.56	0.14
Confusion	−2.0	6.5	0.5	5.6	0.72	0.48

TABLE 2. Wisconsin Card Sorting Test Results for 20 Schizophrenic Patients While Receiving Placebo and While Receiving Amphetamine

Test Measure	While Receiving Placebo Mean	SD	While Receiving Amphetamine Mean	SD	t (df=19)	p
Number of correct responses	75.6	25.9	81.3	22.2	1.78	0.09
Conceptual level (%)[a]	51.7	26.3	56.9	22.6	1.84	0.08
Number of categories achieved	4.0	3.1	4.3	3.4	0.86	0.40
Number of failures to maintain set	1.7	1.7	2.0	1.7	0.81	0.43
Perseverative errors (%)	17.2	7.7	18.0	14.2	0.26	0.80

[a] The percentage of correct responses in runs of three or more.

Data from the Wisconsin Card Sorting Test were analyzed by matched-pair t tests. Results are summarized in table 2. Trends for a significant effect for amphetamine were found for conceptual level (the percentage of correct responses in runs of three or more) and number of correct responses. These were in the predicted direction—i.e., amphetamine improved performance. The number of categories attained and the percent of perseverative errors did not change as a function of amphetamine condition.

Multiple paired t test comparisons between active drug and placebo conditions were performed on the remaining cognitive tasks. No significant changes were present for the total score on the Selective Reminding Test ($t=0.31$, df=11, $p=0.76$), the critical stimuli measure of the Continuous Performance Test ($t=0.24$, df=13, $p=0.81$), the interference measure on the Stroop Color and Word Test ($t=0.68$, df=11, $p=0.58$), or verbal fluency ($t=0.36$, df=11, $p=0.73$). The Understanding Communication test scores improved at the trend level ($t=1.91$, df=11, $p=0.08$). This was due, in part, to the fact that the patients completed more items while receiving amphetamine. Qualitatively defined responders did not differ from nonresponders on any of the difference scores between placebo and active conditions on the cognitive variables (by matched-pair t test).

Matched-pair t tests were used to analyze changes in results of motor tests between active drug and placebo conditions. Motor speed in finger-tapping ($t=2.32$, df=11, $p=0.03$) and trail-making ($t=2.96$, df=11, $p=0.01$) significantly increased while the patients were receiving amphetamine, but no changes were noted in perseveration in designs, go/no go errors, and blink rate ($t<1.33$, df=11, $p>0.21$).

Rotometer data indicated the presence of a significant difference between conditions in the ratio of 360° to 90° movements ($t=3.42$, df=11, $p=0.007$). This difference appeared to be due to an increase in 90° movements (i.e., general activity) during the amphetamine condition. There were no significant differences between the qualitatively defined responders and nonresponders in change scores on any motor task by matched-pair t tests.

Serum levels of amphetamine ranged from 11 to 82 ng/ml. The mean serum amphetamine level for the group was 34.3 ng/ml. Serum amphetamine levels were not significantly correlated with response ($r=-0.13$, $p=0.59$), nor were they correlated significantly with change scores on the POMS. Amphetamine levels were not correlated significantly with any cognitive change scores, including those on the Wisconsin Card Sorting Test. Also, amphetamine level did not correlate significantly with any motor change scores.

Systolic blood pressure increased by 6 mm Hg from placebo to active conditions at the trend level ($t=1.78$, df=14, $p=0.10$) at 1 hour. Pulse rate increased significantly by a mean of 16 bpm from placebo to active drug condition at 4 hours ($t=3.93$, df=14, $p=0.008$).

DISCUSSION

In this study we sought to determine if an acute dose of dextroamphetamine might have positive effects on affect and cognition in schizophrenic patients maintained on a regimen of haloperidol and, if so, what variables might predict such improvements. We based this premise on the rationale that D_1 receptors in the frontal cortex (22) might be indirectly stimulated by amphetamine, resulting in improved affect and cognition, while the potential psychotogenic effects of amphetamine stimulation of subcortical D_2 sites would be prevented by haloperidol blockade (21, 41).

Six of the 21 schizophrenic patients in our study appeared to improve. This was evident in the global ratings by the investigators, ratings of videotapes by clinical research staff, and the self-reports of the patients on the POMS. These results are consistent with a number of open trials of amphetamine that were reviewed by Chiarello and Cole (7) but not with the findings of Casey et al. (42), who noted that a combination of chlorpromazine and dextroamphetamine administered chronically to schizophrenic inpatients resulted in increases in aggressive behavior. Dextroamphetamine doses were higher (60 mg/day) and the neuroleptic doses were substantially lower (300–500 mg/day of chlorpromazine) in the study of Casey et al. than in our present study. The rather low dose of amphetamine we used (0.25 mg/kg) may have been potent enough to improve affect, but the dose of the neuroleptic haloperidol (generally about 1000 to 1500 mg in chlorpromazine equivalents) may have reduced aggression. However, we did not administer amphetamine on a chronic basis, as did Casey et al. Another difference between the studies is the dissimilarity in the D_1/D_2 blockade profiles of haloperidol and chlorpromazine. Because chlorpromazine is a more potent D_1 blocker than is haloperidol (21), the dopaminergic effects of amphetamine at the cortical level may have been attenuated in the study of Casey et al.

The affective changes we observed in patients given amphetamine were similar to those which occur in normal subjects (40). These changes have been thought to be related to stimulation of so-called pleasure centers in the cerebrum. Dopamine is involved in their function (43), and amphetamine, in particular, is rewarding in rats and monkeys (44). The prefrontal cortex is an important site in the pleasure/reward system, as are the ventral tegmental area, nucleus accumbens, and medial forebrain bundle (44, 45). Although amphetamine appears to be a potent dopamine agonist in the prefrontal cortex (46), it also has noradrenergic and serotonergic potentiating effects that may be related to prefrontal function (20).

Amphetamine response could be predicted on the basis of an anatomical measure, VBR, and a dynamic phenomenological measure, spontaneous eye-blink rate. Patients whose VBRs were greater than 7.0 generally improved in our study. This is consistent with several earlier studies. Jeste et al. (15) administered the dopamine agonist apomorphine and found that schizophrenic patients with large VBRs responded most positively. Pandurangi et al. (47) observed that patients with larger VBRs did not worsen during an amphetamine challenge in comparison with patients with smaller VBRs. These results are also consistent with the view that dopaminergic function tends to be lower in patients with high VBRs (18, 48).

Increases in spontaneous eye-blink rate were also strongly associated with a positive response to amphetamine. Blink rate in primates and humans appears to be dependent on dopaminergic activity at the D_2 receptor (49). Its relation to D_1 receptor activity is unknown.

There seemed to be a positive but not robust effect of amphetamine on the Wisconsin Card Sorting Test. Amphetamine might have resulted in a more effective "win-stay" strategy, thus serving to increase the number of correct responses and the conceptual level. These findings might also be consistent with the idea that stimulation of the mesocortical dopaminergic system improves cortical signal-to-noise ratios in terms of information processing and transfer (50). In addition, some of the patients in this study underwent single photon emission computed tomography regional cerebral blood flow scans (51), and preliminary results suggest that amphetamine selectively augmented prefrontal cerebral blood flow during a Wisconsin Card Sorting Test cognitive activation procedure.

We found no differences between the active drug and placebo conditions on other cognitive measures, including those involving attention and memory retrieval. Performance neither improved nor deteriorated. There is debate about the effects that amphetamine has on aspects of cognition in normal subjects (39, 52, 53). In schizophrenia, our results were consistent with those of Kornetsky (54), who also found that amphetamine had little effect on attention in patients with chronic schizophrenia.

Amphetamine appeared to increase the patients' psychomotor speed as well as their gross level of activity as measured by 90° movements. Amphetamine did not appear to produce the "rotational" or circling behavior that is thought to be the result of dopaminergic abnormalities in the striatum (31).

Although our hypothesis leads us to interpret our results in terms of cortical dopaminergic activity (55), another less elaborate explanation cannot be ruled out. It is conceivable that amphetamine simply ameliorated neuroleptic-induced extrapyramidal effects such as akinesia, apathy, and lack of spontaneity (56) by overcoming D_2 blockade.

Another point worth emphasizing is that the magnitude of the positive results on the Wisconsin Card Sorting Test and motor speed, although significant statistically, was not overwhelming. These results come in the context of multiple statistical tests, which, of course, increase the risk of type I error. They were consistent, however, with the a priori hypothesis. Furthermore, serum level of amphetamine did not correlate with change scores on cognitive measures or improvement, although variability in the time that elapsed between amphetamine administration and the drawing of blood may have obscured any relationship.

Historically, it is not clear why dopamine agonists such as amphetamine and L-dopa, which appeared to have clinical promise, have not been investigated more widely. It is possible that the prevailing scientific Zeitgeist, with its emphasis on the dopamine theory of schizophrenia, was not conducive to this work, or perhaps the agonist-related benefits, although significant statistically, were not impressive clinically. Moreover, in some studies, some patients, depending on dose and clinical state, deteriorated. These concerns notwithstanding, the possibility that a dopamine agonist in combination with an antipsychotic drug will benefit some patients with schizophrenia merits further investigation. However, because of the acute nature of the trial and the specialized research environment in which it occurred, it is not appropriate to generalize these findings to other settings or to chronic dosing.

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Use of Neuroleptic-Induced Extrapyramidal Symptoms to Predict Future Vulnerability to Side Effects

George A. Keepers, M.D., and Daniel E. Casey, M.D.

Objective: Susceptibility to neuroleptic-induced extrapyramidal syndromes varies widely, even within age and sex subgroups. Individual vulnerability to extrapyramidal syndromes has been assumed to explain this, but the utility of past history for predicting future occurrence of extrapyramidal syndromes has not been studied extensively. This investigation was undertaken to determine whether patients' previous histories of extrapyramidal syndromes predict future episodes of extrapyramidal syndromes and to compare the importance of this predictive factor with patient age, sex, neuroleptic dose, and anticholinergic dose as predictors of extrapyramidal syndromes. Method: The charts of 62 schizophrenic patients with multiple neuroleptic treatment episodes were reviewed. Extrapyramidal syndromes, neuroleptic drug doses, and anticholinergic drug doses during the first 21 days of each treatment episode were recorded. Results: Previous extrapyramidal syndromes correctly predicted extrapyramidal syndromes in subsequent treatments for 84% of the patients. Variations in neuroleptic potency, neuroleptic dose, and anticholinergic dose partially explained incorrect predictions. Conclusions: These results support the hypothesis that patients with a history of extrapyramidal syndromes are at greater risk for future extrapyramidal syndromes. If confirmed, these results strongly support individual susceptibility as a major predictor of extrapyramidal syndromes and indicate that prophylaxis of extrapyramidal syndromes should be considered for patients who have previously suffered extrapyramidal syndromes from similarly prescribed neuroleptic therapy.

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Difficulty predicting neuroleptic-induced extrapyramidal syndromes has contributed to the controversy surrounding prophylaxis of such syndromes. Without reliable prediction of extrapyramidal syndromes, many patients are unnecessarily treated with prophylactic anti-extrapyramidal medications, increasing the morbidity associated with this procedure (1). We have reported the predictability of dystonia on the basis of patient age, sex, neuroleptic dose, and neuroleptic potency limited by an error rate of 30% (2). This study and clinical experience indicate that even within sex and age subgroups, the propensity for extrapyramidal syndromes varies widely among patients. Individual vulnerability to extrapyramidal syndromes has been assumed to explain this variation; however, the utility of past history for predicting future occurrence of extrapyramidal syndromes has not been studied extensively. This investigation was undertaken to determine whether patients' previous histories of extrapyramidal syndromes predict future episodes of extrapyramidal syndromes and to compare the importance of this predictive factor with patient age, sex, neuroleptic dose, and anticholinergic dose as predictors of extrapyramidal syndromes.

METHOD

The charts of all patients diagnosed with schizophrenia and medicated with multiple neuroleptic treatments at our facility in 1 year were reviewed. The charts of patients who had taken oral or depot neuroleptics, anticholinergics, tricyclic antidepressants, or drug overdoses before admission were excluded. The charts of patients who had received multiple inpatient neuroleptic treatments at our facility within 5 years of the index hospitalization were included in the study. The patients' age and sex were recorded, as were the type and dose of neuroleptic and the type and dose of anticholinergic prescribed during the first 21 treatment days in each hospitalization. To find episodes of extra-

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pyramidal syndromes, the progress notes, nurses' notes, and discharge summaries were reviewed. Extrapyramidal reactions were recorded only if specifically diagnosed and treated. To test for biases in the diagnosis, recording, or treatment of extrapyramidal syndromes, the patients' physicians and hospital wards were registered.

The review found 62 patients with records of multiple treatment episodes. When more than two hospitalizations were found (N=24), the two hospitalizations with the most similar treatments were chosen on the basis of specific neuroleptic drug and dose. The mean daily neuroleptic dose was calculated in chlorpromazine equivalents (3) for each patient during both treatments. The anticholinergic activities of neuroleptic and antiparkinsonian drugs were expressed in benztropine equivalents (4, 5). A ratio of dopamine blocking potency and anticholinergic activity (the ratio of chlorpromazine equivalents to benztropine equivalents) was calculated by dividing a patient's mean daily neuroleptic dose by his or her mean daily anticholinergic dose (2). Doses reported are those which were in effect preceding the development of an extrapyramidal syndrome. Thus, benztropine equivalents given do not include anticholinergics given for treatment of an extrapyramidal syndrome after it occurred. They do include anticholinergics given prophylactically before development of any extrapyramidal syndromes.

Presence of extrapyramidal syndromes in earlier treatments was tested as a predictor of extrapyramidal syndromes in subsequent treatments. Additionally, a linear discriminant function based on previous history of extrapyramidal syndromes, age, sex, anticholinergic dose, neuroleptic dose, and the ratio of chlorpromazine equivalents to benztropine equivalents to predict extrapyramidal syndromes in the index treatment was calculated. The accuracy of the discriminant function without previous history was compared with predictions based solely on previous history. Cases in which past history did not predict extrapyramidal syndromes correctly were studied for other factors influencing extrapyramidal syndromes. Due to the small number of subjects in the incorrect prediction group, the Wilcoxon signed rank test was used for comparisons.

RESULTS

During the first treatment, 36 (58.1%) of the 62 patients had extrapyramidal syndromes: dystonia occurred in 18 (29%), parkinsonism affected 18 (29%), and akathisia occurred in 13 (21%). Fourteen (38.9%) of the 36 patients with extrapyramidal syndromes had more than one syndrome.

The patients' second treatment occurred, on the average, 1.2 years after the first. During the second treatment neuroleptic therapy produced extrapyramidal syndromes in 34 (54.8%) of the 62 patients. Dystonia occurred in 11 (17.7%), parkinsonism in 23 (37.1%), and akathisia in 17 (27.4%). Fourteen (41.2%) of the 34 patients had more than one extrapyramidal syndrome. Prophylactic anticholinergics were given to 20 (32.3%) of the 62 patients.

Thirty of the 34 patients with extrapyramidal syndromes in the second treatment had had extrapyramidal syndromes in their first treatment, yielding a sensitivity of 88.2% (95% confidence limits: 94.1%–63.4%). Twenty-two of the 28 patients without extrapyramidal syndromes in their second treatment had not had extrapyramidal syndromes in their first, yielding a specificity of 78.6% (95% confidence limits: 92.3%–54.7%). The sensitivity for prediction of an extrapyramidal syndrome subtype was less: eight of the 11 patients with dystonia in the second treatment had had dystonia in the first (72.7%) (95% confidence limits: 99.0%–46.4%); seven of the 17 patients with akathisia in the second treatment had had akathisia in the first (41.2%) (95% confidence limits: 64.6%–17.8%); and 12 of the 23 patients with parkinsonism in the second treatment had had parkinsonism in the first (52.2%) (95% confidence limits: 72.6%–31.8%). There were correspondingly higher specificities: 41 of the 51 patients without dystonia in the second treatment had not had dystonia in the first (80.4%) (95% confidence limits: 91.3%–69.5%); 39 of the 45 patients who did not have akathisia in the second treatment had not had akathisia in the first (86.7%) (95% confidence limits: 96.6%–76.8%); and 33 of the 39 patients who did not have parkinsonism in the second treatment had not had parkinsonism in the first (84.6%) (95% confidence limits: 95.9%–73.3%).

Thus, previous history of extrapyramidal syndromes correctly predicted extrapyramidal syndromes during subsequent treatment in 52 (83.9%) of the patients and was more successful than the discriminant function with previous history excluded, which predicted correctly in 42 (67.7%) of the cases ($\chi^2=15.9$, df=3, $p<0.001$). F statistics from the discriminant function indicated the relative importance of previous history of extrapyramidal symptoms (F=49.9, df=60, $p<0.001$), age (F=4.90, df=60, p=0.31), sex (F=5.46, df=60, p=0.02), chlorpromazine equivalents/day (F=0.147, df=60, p=0.70), benztropine equivalents/day (F=2.98, df=60, p=0.09), and the ratio of chlorpromazine equivalents to benztropine equivalents (F=0.303, df=60, p=0.58) as predictors of extrapyramidal syndromes (see table 1).

Presence of dystonia during the first treatment correctly predicted dystonia during the second treatment in 49 (79.0%) of the patients. Previous parkinsonism correctly forecast parkinsonism during the second treatment in 47 (75.8%) of the patients. A history of akathisia was predictive in 45 (72.6%).

A history of extrapyramidal syndromes incorrectly predicted subsequent extrapyramidal syndromes in 10 (16%) of the patients. Marked differences in the ratio of chlorpromazine equivalents to benztropine equivalents between treatments with and without extrapy-

TABLE 1. Age, Sex, and Neuroleptic Doses of 62 Schizophrenic Patients With Multiple Neuroleptic Treatment Episodes With and Without Extrapyramidal Syndromes

Time and Presence or Absence of Extrapyramidal Syndrome	Age		Men		Chlorpromazine Equivalents/Day		Benztropine Equivalents/Day		Ratio of Chlorpromazine Equivalents to Benztropine Equivalents
	Mean	SD	N	%	Mean	SD	Mean	SD	
First treatment	30.1	9.9	32	51.6	853	712	0.73	1.12	1168
Syndrome occurred (N=36)	28.2	8.4	21	58.3	897	683	0.48	0.85	1869
Syndrome did not occur (N=26)	32.9	11.4	11	42.3	791	760	1.09	1.36	726
Second treatment^a	—	—	—	—	1119	1047	1.31	1.69	854
Syndrome occurred (N=34)	27.7	8.4	22	64.7	1166	1114	0.99	1.58	1178
Syndrome did not occur (N=28)	33.1	11.0	10	35.7	1062	978	1.71	1.76	621

[a] The difference between the patients with and without extrapyramidal syndromes was not significant for chlorpromazine equivalents per day (t=0.384, df=122, p=0.70), benztropine equivalents per day (t=1.73, df=122, p=0.09), or the ratio of the two (t=0.55, df=122, p=0.58).

TABLE 2. Neuroleptic Doses of 10 Patients Whose Previous History of Extrapyramidal Syndromes Failed to Predict Future Syndromes

Patient and Presence or Absence of Extrapyramidal Syndrome	Chlorpromazine Equivalents/Day	Benztropine Equivalents/Day	Ratio of Chlorpromazine Equivalents to Benztropine Equivalents
Patient 18			
Syndrome did not occur	371	0.816	454
Syndrome occurred	1500	0.236	6,350
Patient 25			
Syndrome did not occur	1140	0.000151	7,580,000
Syndrome occurred	667	0.000088	7,590,000
Patient 26			
Syndrome did not occur	1240	2.9400	420
Syndrome occurred	792	0.0001	7,200,000
Patient 42			
Syndrome did not occur	422	1.410	299
Syndrome occurred	714	0.008	84,900
Patient 43			
Syndrome did not occur	449	0.193	2,320
Syndrome occurred	1210	0.014	84,900
Patient 44			
Syndrome did not occur	415	3.9900	104
Syndrome occurred	750	0.0010	7,580,000
Patient 46			
Syndrome did not occur	1450	4.0000	362
Syndrome occurred	500	0.0001	7,580,000
Patient 49			
Syndrome did not occur	1060	3.630	291
Syndrome occurred	1360	7.520	181
Patient 50			
Syndrome did not occur	500	0.00008	6,320,000
Syndrome occurred	450	0.00529	84,900
Patient 59			
Syndrome did not occur	420	0.0487	8,630
Syndrome occurred	450	0.0071	84,900

ramidal syndromes were noted (p=0.05, Wilcoxon signed rank test) (see table 2). Neuroleptic dose was higher but not significantly so (p=0.65, Wilcoxon signed rank test) in the treatments when extrapyramidal syndromes occurred. Patients received higher anticholinergic doses during treatments when extrapyramidal syndromes did not occur, but the difference was not significant (p=0.07, Wilcoxon signed rank test).

Lesser differences between treatments when extrapyramidal syndromes did or did not occur were found in all 62 patients (see table 1).

Potential biases in selection of the second neuroleptic treatment were examined by separate analyses of the patient groups with two treatments and those with more than two treatments. No significant differences between the two groups in prediction of extrapyramidal syndromes by previous history were found.

The data were also examined for possible biases in reporting of extrapyramidal syndromes by physician and by ward. Five staff physicians provided 99 (79.8%) of the treatments for 60 patients. Seven other staff physicians each treated from one to five of the remaining patients (25 treatments for 23 patients). Extrapyramidal syndromes reported by the five most active physicians varied from 72.7% to 50.0%. Reported frequencies of extrapyramidal syndromes did not differ significantly between physicians ($\chi^2=1.914$, df=4, p=0.75). The rates of extrapyramidal syndromes in the 17 patients who were treated twice by the same physician were 58.8% (10 patients) in the first treatment and 64.7% (11 patients) in the second. The rates of extrapyramidal syndromes in the 45 patients who had different physicians for the two treatments were 57.8% (26 patients) in the first treatment and 51.1% (23 patients) in the second. These rates did not differ significantly (first treatment, $\chi^2=0.006$, df=1, p=0.94; second treatment, $\chi^2=0.921$, df=1, p=0.34).

Patients were hospitalized on one of two hospital psychiatric units. Seventy-six (68.5%) of the 111 treatments that occurred entirely on a single ward (for 51 of the patients) took place on the more active unit. Extrapyramidal syndromes were reported for 45 (59.2%) of the treatments on this unit (31 patients) versus 18 (51.4%) of the treatments on the other unit (15 patients). The reported rates of extrapyramidal syndromes did not differ significantly between the two units ($\chi^2=0.591$, df=1, p=0.44).

DISCUSSION

These results support the hypothesis that patients with a history of extrapyramidal syndromes are at greater risk for future extrapyramidal syndromes. However, caution in interpreting the results is warranted by the retrospective nature of the data, the small number of patients studied, and possible biases in rating extrapyramidal syndromes. Examination of rates of extrapyramidal syndromes recorded by ward and by physician failed to show any bias, but we are not able to rule out bias due to clinicians' knowledge of the patient. Some reassurance on this point can be taken from the finding that the rates of extrapyramidal syndromes in the group of patients treated by the same clinician on the same ward twice did not differ from the rates in the group treated by different doctors for their second treatment.

Additionally, some prudence is justified in considering the neuroleptic dose comparisons reported here because reported dose equivalencies (3) vary considerably. These equivalencies in combination with the anticholinergic equivalencies are used to provide a quantitative measure to account for the clinical observation that drugs such as haloperidol and chlorpromazine produce different rates of extrapyramidal syndromes. This measure has been validated in previous work (2).

The findings are consistent with experiments in nonhuman primates demonstrating variable individual susceptibility to extrapyramidal syndromes (6). Variations in dopamine, acetylcholine, γ-aminobutyric acid (GABA), or drug metabolism may account for these differences (7). Microanatomical variation in the basal ganglia might also explain deviations in susceptibility to drug-induced extrapyramidal syndromes. Alternatively, primate experiments have suggested that neuroleptic exposure produces reverse tolerance to extrapyramidal syndromes (8).

Although less predictive than previous history, age, sex, and anticholinergic dose were also effective prognostic indicators. These results are consistent with earlier work that demonstrated relationships between these variables and extrapyramidal syndromes (9, 10). Our work concerned with the prediction of dystonia (2) also confirmed the importance of these variables. The error rate in that investigation (30%) was similar to the 33% error rate for the discriminant function in this study.

Differences in anticholinergic dose and ratio of chlorpromazine equivalents to benztropine equivalents largely accounted for the 10 cases where a history of extrapyramidal syndromes failed to predict future extrapyramidal syndromes. These differences were primarily due to prescription of prophylactic anticholinergics during the symptom-free treatment episode. This finding is in agreement with previous work of ours that supports the effectiveness of anticholinergic prophylaxis in preventing neuroleptic-induced extrapyramidal syndromes (9).

These data suggest that prophylaxis of extrapyramidal syndromes and/or low-dose neuroleptic treatment can protect patients from extrapyramidal syndromes yet spare some patients unnecessary prophylactic anticholinergic treatment. If confirmed, these results strongly support individual susceptibility as a major predictor of extrapyramidal syndromes and indicate that prophylaxis of extrapyramidal syndromes should be considered for patients who have previously suffered extrapyramidal syndromes from similarly prescribed neuroleptic therapy.

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Christian Psychiatry: The Impact of Evangelical Belief on Clinical Practice

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Objective: The authors surveyed psychiatrists in the Christian Psychiatry movement to assess the role of religious belief in their practices. Method: The psychiatrists were members of the Christian Medical and Dental Society; questionnaires were sent to 260, and usable responses were received from 193. The subjects were asked about demographic and practice variables, "born again" religious experiences, group cohesion, and beliefs about using the Bible and prayer in treatment. Results: The respondents were somewhat more religious than Americans overall, who are themselves more religious than most psychiatrists. Nearly all reported having been "born again," after which they generally experienced a decrease in emotional distress. There was a significant difference in the respondents' affiliative feelings toward psychiatrists in the Christian Psychiatry movement and other psychiatrists. For acute schizophrenic or manic episodes, the respondents considered psychotropic medication the most effective treatment, but they rated the Bible and prayer more highly for suicidal intent, grief reaction, sociopathy, and alcoholism. Whether or not a patient was "committed to Christian beliefs" made a significant difference in whether the respondents would recommend prayer to the patient as treatment. About one-half said they would discourage strongly religious patients from an abortion, homosexual acts, or premarital sex, and about one-third said they would discourage other patients from these activities. Conclusions: Many studies have suggested a need for more sensitivity to religious issues by psychiatrists, and this study provides systematic findings on one approach. It remains important to evaluate ways in which a religious perspective can be related to clinical practice and what benefits and problems may derive from such a relationship.

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A recent resurgence in religious commitment in the United States, including fundamentalism (1), may lead psychiatry to reconsider the place of religious issues in clinical practice. This is particularly relevant to the impact of Christian Psychiatry, a broad-based national movement of psychiatrists who are evangelical Christians. Although most of its adherents are not formally affiliated among themselves, the orientation of this movement is expressed in beliefs espoused by the Christian Medical and Dental Society, which has 7,500 members, 260 of whom are psychiatrists or physicians in psychiatry residency training. Applicants must sign a statement acknowledging "the final authority of the Bible as the word of God . . . , the presence and power of the Holy Spirit in the work of regeneration . . . , [and] the everlasting blessedness of the saved and the everlasting punishment of the lost."

Because of the intensity of religious commitment in the Christian Medical and Dental Society, it seemed useful to make an independent assessment of the role religious belief plays in the clinical practice of psychiatrists who are members of the society. We also hoped to provide a better understanding of how strong religious belief can affect mental health care.

METHOD

We established an agreement with officers of the psychiatry section of the Christian Medical and Dental Society that we would conduct a study for the purpose

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of familiarizing the mental health field with Christian Psychiatry by means of objective findings. A representative group of members was initially interviewed, and a mailing was then sent to the 260 potential respondents. It included a letter from the president of the psychiatry section which explained that only summary data would be published and that identifiable information on respondents would not be retained or reported. A 121-item codeable questionnaire was included in the mailing, to be returned anonymously. From this and follow-up correspondence, 193 usable questionnaires were returned, representing a 74% response rate.

The questionnaire included items on demography and practice, many drawn from the report on a survey of American psychiatrists that was conducted by APA (2). Additional items on religion were drawn from a report from a Gallup poll of a probability sample of 1,553 Americans (3). Responses to items were given on a 5-point scale, from 1, for "not at all," to 5, for "very much."

The subjects were asked to retrospectively assess their psychological state immediately before having "been born again or having . . . an intense religious experience that changed your outlook on life." They were then asked to make the same assessment for the month immediately after that experience. They rated eight items, such as, "I felt nervous and tense," on a 5-point scale (maximum possible total=40). This neurotic distress measure has been reported previously (4, p. 33) to have a high level of internal consistency; it correlates significantly with measures of behavior in zealous religious and self-help groups, with contemporary measures of distress in related groups, and inversely with the General Well-Being Schedule of the National Center for Health Statistics (5).

Five items assessing group cohesiveness, such as, "They care for me" and "I enjoy being part of their activities," were also used. A high internal consistency among these items and a significant correlation between the items and behavior in zealous groups have been reported (4, p. 32, and 5). Respondents used the 5-point scale for each item to rate their affiliative feelings toward two target groups, the 10 Christian Psychiatrists they know best and the 10 psychiatrists they know best who are not members of the movement. The maximum possible total score was 25.

The respondents were asked to give their estimation on the 5-point scale of the effectiveness of each of three possible interventions in treating each of seven diagnoses, such as alcoholism. The three interventions were the Bible and prayer, insight psychotherapy, and psychotropic medications.

The role of religion in the respondents' clinical practice was addressed in two ways. The respondents were first asked to indicate what portion of committed Christian believers with given diagnoses—schizophrenia, depressive neurosis (dysthymia), and alcoholism—they would treat with each of three modalities: a specified conventional treatment, insight psychotherapy, and prayer (by the patient). They were then asked what portion of nonbelievers they would treat with each of the modalities. The role of religion was further addressed by asking the respondents whether or not they would suggest to a committed Christian patient that he or she act otherwise if he or she were about to act contrary to evangelical Christian creed. Three examples of such acts were given: planning an abortion, engaging in homosexual acts, and engaging in premarital sex. The respondents were then queried as to how they would respond to the same three situations if the patient were not a committed Christian believer.

Some respondents did not answer every question, so the total number of subjects used for calculating percentages varies among the questions asked.

RESULTS

Demographic and Professional Background

The respondents' mean±SD age was 49.1±12.7 years, and 172 (89%) were male. Of the 179 who were not currently in residency training, 175 (98%) had completed psychiatric residency, and 121 (68%) were Board certified. The most common primary work setting was private practice (N=100, 52%), followed by medical school/university (N=23, 12%) and mental health clinic (N=20, 10%). These findings are similar to those reported for American psychiatrists overall, according to APA biographical data (2).

The mean±SD length of membership in the Christian Medical and Dental Society was 15±12.4 years. Over half of the respondents (N=112, 59%) had faculty appointments at medical schools, and 168 (88%) were APA members. The respondents were geographically dispersed and lived in 35 states; the states with more than 10 respondents each were California, Texas, Pennsylvania, and Michigan.

Religious Beliefs

Data gathered from the responses to the questions on religious beliefs were compared with figures from Gallup poll data (3). They revealed a moderately stronger religious commitment among the respondents than among Americans overall. For example, 78% of the respondents (N=145) indicated that they believe in a personal God who "rewards and punishes" them for their actions, as do most (69%) of the general population; 98% (N=188) stated they believe in the Devil (versus 70% of the general population). The respondents' religious orientation was further reflected in three items used by Gallup as strict criteria for defining evangelical Christians among the general population: 182 (96%) said they had been "born again" (versus 40% of the general population), 183 (96%) acknowledged having encouraged someone to accept Jesus as a savior (48% in the general population), and 80 (43%) stated that every part of the Bible is the actual word of God,

TABLE 1. Ratings of Effectiveness of Three Treatments by 193 Psychiatrists Who Were Members of the Christian Medical and Dental Society

	Rating of Effectiveness (1=not at all, 5=very much)						ANOVA for Repeated Measures		
	Psychotropic Medication		Bible and Prayer		Insight Psychotherapy				
Psychiatric Syndrome	Mean	SD	Mean	SD	Mean	SD	F	df	p<
Acute schizophrenic episode	4.8	0.6	1.7	0.9	1.5	0.6	1,227	2, 372	0.001
Acute manic episode	4.9	0.4	1.7	0.9	1.4	0.6	1,614	2, 372	0.001
Suicidal intent	3.2	1.1	3.5	1.1	3.2	1.0	6.39	2, 372	0.01
Grief reaction	2.1	0.8	4.1	0.9	3.4	0.9	271.6	2, 372	0.001
Sociopathy	1.4	0.7	2.8	1.2	2.1	0.9	125.2	2, 372	0.001
Alcoholism	1.9	0.8	3.6	1.1	2.7	0.9	182.0	2, 374	0.001
Depressive neurosis	3.1	1.0	3.5	1.1	3.8	0.9	19.4	2, 374	0.001

to be taken literally (37% in the general population). Regarding religious issues that may arise in clinical practice, a large majority felt the following practices are wrong: homosexual relations between consenting adults (N=166, or 88%, versus 62% in the general population), sexual relations before marriage (N=159, or 86%, versus 50%), and abortion on demand (N=187, or 99%, versus 87%).

The subjects' ratings of their emotional distress before and after their "born again" experiences were significantly different. Their mean±SD score on the eight-item measure was 11.0±7.0 for immediately before the experience and 8.2±4.4 for the month afterward (t=8.1, df=178, $p<0.001$; t test for repeated measures, two-tailed). This decline in distress is illustrated by responses to a typical item: whereas 34 (19%) of the respondents felt quite anxious (4 or 5 on the 5-point scale) before their "born again" experiences, only two (1%) felt that way during the month afterward ($\chi^2=31.6$, df=1, $p<0.001$).

Group Cohesiveness

The strength of the respondents' cohesiveness with the Christian Psychiatry movement was evident in their mean score for affiliative feelings toward the 10 Christian Psychiatrists they knew best (18.5±3.4), which was considerably higher than the score for affiliative feelings toward the psychiatrists whom they knew best who were not members of the movement (13.6±2.9) (t=15.2, df=171, $p<0.001$; t test for repeated measures). This difference is illustrated by a typical item, "Do you like being part of their activities?" to which 107 (61%) of the respondents answered 4 or 5 for Christian Psychiatrists and only 27 (15%) answered that way for the psychiatrists who were not Christian Psychiatrists. Furthermore, we compared this difference in affiliative feelings toward insiders and outsiders to differences between members and nonmembers in other highly cohesive groups. The mean difference in total scores on the cohesiveness scale between insiders and outsiders (4.9±4.3) was not significantly different from that shown for 100 participants in a highly cohesive, long-term treatment program for addicted physicians (4.8±5.4), reported on previously (6). It was, however, significantly less than that shown by 237 members of a zealous religious sect who lived communally (7.6±5.2) (t=5.6, df=407, $p<0.001$) (7).

Belief in Therapeutic Effectiveness of Bible and Prayer

The respondents were asked to rate the relative effectiveness of three interventions in treating the psychiatric problems of "Christian believers," using the 5-point scale. For both an acute schizophrenic episode and an acute manic episode, they rated psychotropic medication as more effective than either Bible and prayer or insight psychotherapy (see table 1). On the other hand, Bible and prayer was scored as the most effective modality for suicidal intent, grief reaction, sociopathy, and alcoholism, although not for depressive neurosis (see table 1).

Religious Influence on Clinical Practice

The respondents were asked what proportion of patients with specific diagnoses they would treat with each of three therapeutic approaches. It was explained that the approaches need not be exclusive, so the total percentages assigned to the three approaches could exceed 100%. As illustrated in table 2, the respondents reported they would use prayer for about one-half the patients who were "committed to Christian beliefs" but for less than one-fifth of patients from a "nonbelieving Christian background." On the other hand, there was no significant difference between the proportions of believing and nonbelieving patients to which they would apply conventional therapeutic approaches.

In a second set of questions, they were queried about whether they would "suggest that their patient act otherwise" if he or she were a Christian believer planning to engage in an abortion, homosexual acts, or premarital sex. The psychiatrists' responses differed significantly according to whether the hypothetical patient were a committed Christian or not: abortion, 49% versus 28% ($\chi^2=16.4$, df=1, $p<0.001$); homosexual acts, 56% versus 32% ($\chi^2=23.4$, df=1, $p<0.001$);

TABLE 2. Relationship of Treatment Choice to Patients' Christian Beliefs for 193 Psychiatrists Who Were Members of the Christian Medical and Dental Society

	Proportion of Patients for Whom Psychiatrists Would Prescribe Treatment (%)						
	Patients "Committed to Christian Beliefs"		Patients From "Nonbelieving Christian Backgrounds"		Two-Tailed t Test for Repeated Measures		
Diagnosis and Treatment	Mean	SD	Mean	SD	t	df	p
Schizophrenia							
Neuroleptics	97.3	10.3	97.5	9.6	−1.4	189	n.s.
Psychotherapy	56.0	38.7	55.5	38.7	0.8	189	n.s.
Prayer by the patient	31.7	39.2	8.6	24.2	9.0	189	<0.001
Depressive neurosis							
Antidepressants	60.4	25.8	61.9	26.6	−2.4	189	<0.05
Psychotherapy	90.4	19.5	89.3	21.2	1.5	188	n.s.
Prayer by the patient	52.0	40.3	13.5	28.2	13.7	188	<0.001
Alcoholism							
Alcoholics Anonymous	92.0	17.4	93.9	15.0	−2.2	188	<0.05
Psychotherapy	63.9	33.3	63.5	33.5	0.8	188	n.s.
Prayer by the patient	59.6	41.3	19.8	34.5	13.5	188	<0.001

premarital sex, 51% versus 26% ($\chi^2=25.5$, df=1, $p<0.001$).

We then examined the relationship between the respondents' willingness to promote Christian beliefs in therapy and the intensity of their ties to the Christian Psychiatry movement. We performed analyses to ascertain predictors of a respondent's intervention if a patient were planning an abortion, homosexual acts, or premarital sex. A variable was generated that consisted of the number of activities (of the three listed) the respondent would suggest patients avoid if they are Christian believers. This variable was used as a criterion in two stepwise multiple regression analyses.

In the first analysis, five aspects of religious belief were used as predictors (belief in the Devil, three items from the Gallup poll used to define evangelical belief, and the total score for items reflecting belief in the therapeutic effectiveness of prayer). In the second analysis, we added five variables reflecting affiliation with Christian Psychiatrists rather than other psychiatrists (the difference between affiliative feelings toward 10 Christian Psychiatrists and other psychiatrists on the five cohesion items) and not being Board certified. In each stage of the two regression analyses, predictors were entered into the regression equation only as long as they each accounted for a portion of the variance significant at the $p=0.05$ level. In all, the religious belief items predicted 18% of the variance in the respondents' willingness to intervene in behavior that violated evangelical Christian creed; with the addition of the affiliation variable, 33% of this behavior was predicted. These findings support the hypothesis that feelings of affiliation to the Christian Psychiatry movement were strong and significant predictors of the practitioner's enforcement of Christian beliefs.

The following clinical vignette illustrates how a period of psychiatric distress might contribute to the genesis of a career in Christian Psychiatry, an experience that was often reported. It also shows how practitioners often draw on their interpretation of Biblical passages as an aid in treating patients.

Clinical Vignette

Dr. A, now 50 years old, came from a church-going background but grew up with little personal interest in religion. While in college, however, during a period of depression he decided to participate in a Bible class to find solace. On occasion, during the closing prayer of the class he suddenly felt intensely that he was being born again in Christ. Afterward he embarked on a plan to combine his religious commitment with medical practice. This course was not without conflict, however, as he was reprimanded later during his residency for engaging a patient in prayer. Dr. A currently admits patients to a private psychiatric hospital, many of whose staff are "Christian-oriented." He stated that his therapeutic approach is a conventional one but that when appropriate he goes further, by using Christian beliefs. He pointed out, however, that he has refused to "lay on hands" when occasionally asked to do so by a patient. Although Dr. A does not promote himself as a Christian Psychiatrist, many of his patients are referred to him because they have strong religious beliefs and want to be treated by someone with similar beliefs. When asked to give a clinical example that illustrates his work, Dr. A described his experience with a 41-year-old woman, a devout Christian, whom he diagnosed as having a single episode of severe major depression with psychosis (*DSM-III-R* code 296.24). The patient had no prior history of mental illness, and her symptoms were apparently precipitated by the suicide of her teen-age daughter 2 months before. Dr. A elected to hospitalize her and treat her with a tricyclic and a neuroleptic. In therapeutic sessions in the hospital, the patient was unable to express her feelings of depression and anger. Initially, Dr. A did not allow her to bring her Bible into these sessions because he feared she would find a passage such as the one in which Judas hanged himself and would do likewise herself. After the psychosis abated, however, he thought it was important for her to fully experience her grief and anger over the loss of her child. He therefore read specific citations from the New Testament with her, ones which showed that God allows justified anger and that a bereft person should go through a period of grief. He used these citations to help her justify the expression of feelings she had found difficult to acknowledge. This, he reported, allowed her to work through these feelings and experience relief of her guilt by the time of her discharge from the hospital after 6 weeks.

DISCUSSION

The study of a social movement, such as Christian Psychiatry, inevitably has limitations in design. We learned from numerous sources that many psychiatrists in addition to those in the Christian Medical and Dental Society are evangelical Christians, but they were not accessible in a systematic way. Also, respondents' self-assessments, because they are subjective and often retrospective, do not necessarily accurately reflect their actual behavior at another time. For this reason, subsequent studies with on-site observation and assessment of therapeutic outcome are needed. In addition, the questionnaire, while directed at an understanding of the role of religious belief in the respondents' professional lives, was phrased so as not to offend their religious sensibilities. Nonetheless, given the potential role of religion in the work of certain clinicians, we felt it important to conduct such a survey.

The comparison revealed many aspects of the movement. In terms of demographics and practice variables, the respondents were similar to psychiatrists overall, but they were more strongly religiously oriented than the population overall. This latter difference, however, should be considered in light of a comparable, perhaps greater, disparity in belief between psychiatrists in general and the overall population. Whereas 56% of psychiatrists have been found to be agnostic or atheist (8), only 5% of the general public do not believe in God or a higher power (3). Psychiatrists' general lack of concern for religious matters is also evident in a review of major psychiatric journals conducted by Larson et al. (9), which revealed that only 3% of published articles include a quantified religious variable. This is a rather small percentage considering how widespread religious belief is and the degree to which it can affect the cognitive issues relevant to both psychopathology and psychotherapeutic rehabilitation. The discrepancy between psychiatrists' beliefs and those of their patients is also underlined by a recent study by Kroll and Sheehan (10), who found that 95% of a group of hospitalized psychiatric patients believed in God and a comparably large proportion espoused related religious beliefs. Indeed, the need for sensitivity to religious needs is further evident in the findings from the Epidemiologic Catchment Area Program; of the subjects who had turned to either mental health professionals or clergy for psychiatric assistance, one-third had sought help from the clergy (11). These findings may help to explain the perceived need for religious sensitivity that the Christian Psychiatry movement seeks to meet. Indeed, the emergence of nonprofessional ideology to close gaps in psychiatric care has numerous parallels in other, non-Christian movements (12).

The incorporation of religious belief into treatments used in psychiatric practice is, however, a step beyond sensitivity to patients' beliefs. In taking such a step, the practitioner must depart from the norms for treatment learned in the officially sanctioned specialty training. This alteration may be understood by recourse to a model described by Galanter (4) for religious influence. An intense religious experience that yields relief from emotional distress initially serves as a nidus for engaging commitment; indeed, 96% of our respondents said they had had "born again" experiences. Typically such events are followed by a decline in neurotic distress, an experience also reported by our respondents. Beliefs shared by a reference group are then acquired. This reference group provides a cognitive framework for behavior change. Here, too, our respondents came to espouse a set of strongly held beliefs, rooted in the Bible and promoted by born-again Christians; these shared beliefs legitimized their adoption of new standards of behavior. Finally, a convert must become engaged in a cohesive group that sustains his or her involvement with the movement and that determines consensual norms. For our respondents, this cohesiveness was considerable; it was comparable to that felt among members of a strongly affiliated peer-led therapeutic program for addicted physicians (6).

The fact that some responses were retrospective underlines the importance of contemporaneous studies of mental health practice relative to religious beliefs. It points further to the importance of effective collaboration of psychiatric researchers with parties who apply religious belief to mental health problems. Although we know of no other professional organization for "born-again" psychiatrists outside the Christian Medical and Dental Society, there are, no doubt, many other nonaffiliated practitioners with strong religious views. Clearly, practitioners in a variety of other denominations are worthy of study as well.

Our respondents felt that pharmacotherapy was considerably more effective than other modalities for treating major mental illness. Insight psychotherapy, however, whose effectiveness is more difficult to demonstrate, was not perceived as being as effective as the Bible and prayer. About half of the respondents were prepared to actively discourage believing Christian patients who engaged in homosexuality or premarital sex or were planning an abortion, and almost a third would do the same for nonbelievers.

To what extent does the advice of Christian Psychiatrists have a greater impact than the suggestions of practitioners with strong liberal nonreligious orientations? This question in itself merits study. Clearly, we are dealing with the strong and apparently long-term commitment of these practitioners.

In its recent history, psychiatry has emerged from a tradition of empirical science strongly influenced by a materialist, positivist perspective. As evident in such works as *The Future of an Illusion* (13), Freud was skeptical of religious belief and perceived it as akin to neurosis, a view that has been influential in shaping the contemporary psychiatric world view. In actuality, as Bergin (14) pointed out, there does not appear to be empirical support for this position. Furthermore, an appreciable increase in contemporary religious commitment, in particular in evangelical Christian belief, now suggests greater psychiatric attention to religious issues, in contexts as diverse as the college campus (15), the household (11), and the mental hospital (10). To address this issue, APA has recently approved guidelines regarding possible conflict between psychiatrists' religious commitments and psychiatric practice (16). These address concerns about the need for sensitivity in treatment to patients' religious beliefs.

From an anthropological perspective, the infusion of a religious orientation into practice may be considered akin to indigenous healing, and studies using control subjects, such as those by Kleinman and Gale in Taiwan (17) and Uyanga in Nigeria (18), reveal that subjects who receive faith healing report material benefit from both somatic and psychogenic symptoms. The full import of such reports, however, remains to be elucidated. For example, Pattison et al. (19) evaluated persons who reported relief from a variety of disorders through fundamentalist religious experience and found that they exercised a high degree of denial in the perception of their illnesses and were often unaware of the persistence of their organic pathology. With psychiatric problems, many of which are subjective, denial of distress may at times be akin to cure. The question must be raised, however, of to what degree and in what way a psychiatrist should incorporate a religious perspective into clinical practice.

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How Do HMOs Reduce Outpatient Mental Health Care Costs?

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Objective: Because previous studies of differences in utilization of mental health care services have had important limitations, it is not clear if their findings that health maintenance organization (HMO) outpatient mental health care costs less than fee-for-service care are due to less access, less intensive care per user, or selective enrollment of healthier people by HMOs. Therefore, the authors used data from the National Institute of Mental Health Epidemiologic Catchment Area (ECA) study to examine differences in the prevalence of psychiatric disorder and differences in the use of outpatient mental health services for adults enrolled in HMO or fee-for-service health insurance plans. Method: The subjects were an ECA community sample obtained from East Los Angeles and West Los Angeles. This sample included a large number of Hispanic subjects. The subjects were categorized according to their responses to a 5-item battery on insurance as Medicare enrollees, members of private fee-for-service plans, Medicaid enrollees, members of an HMO, and uninsured. The presence or absence of psychiatric disorders was determined by using the NIMH Diagnostic Interview Schedule. Both users and nonusers of mental health services were studied. Results: The HMO and fee-for-service plans had similar prevalence of psychiatric disorder and similar access to specialty mental health care. However, HMO enrollees had significantly fewer visits per user to providers of specialty care. Conclusions: The most likely explanation for lower mental health care costs in HMOs is a less intensive style of care for a comparably sick population.

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Health maintenance organizations (HMOs) represent the current major alternative to coverage by fee-for-service health insurance in the United States and are likely to increase their share of the U.S. health care system in the future. Previous studies (1, 2) have shown that HMOs reduce expenditures for mental health services. However, it has not been determined whether HMOs control such costs by excluding from enrollment patients with serious psychiatric disorders or by impeding access to mental health services for those enrollees with such disorders. If HMOs control expenditures through restricted enrollment or access, then they might not be able to control expenditures if their enrollment were expanded to include people with psychiatric disorders (e.g., mandating HMOs as a model for Medicaid). Further, for people with psychiatric disorders enrolled in an HMO, any restriction in access could result in poorer outcomes (e.g., increased morbidity and increased societal costs).

Previous studies have compared the mental health of HMO and fee-for-service enrollees using either psychiatric diagnoses assigned by the provider (e.g., claims forms) or global scales of psychological distress. These studies have reached conflicting conclusions. Those relying on measures of psychological distress (2) have found that the mental health statuses of HMO and fee-for-service enrollees were similar. Studies of diagnoses assigned to the individuals using services under these two types of insurance (3), however, have suggested that HMOs enroll a less mentally ill population than fee-for-service plans. Neither type of study has compared enrolled populations (both users and nonusers) by prevalence of psychiatric disorder determined independently of the treating provider.

Studies of use of mental health services by enrollees in HMO and fee-for-service plans have also reached

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conflicting conclusions. Early studies (4–7) found that HMO members were more likely than fee-for-service plan enrollees to use outpatient mental health services. Diehr et al. (1) found a higher proportion of enrollees using outpatient mental health services in a prepaid plan (8.9%) than in a fee-for-service plan (5.4%). Studies based on the RAND Health Insurance Experiment (2, 8) found a similar annual probability of using mental health services but also found that, over several years, enrollees in the HMO plans were more likely than those in comparable fee-for-service plans to use these services. Other studies, including a reanalysis of the data of Diehr et al. (9, 10), have found no difference in the annual probability of using mental health services between HMO and fee-for-service enrollees. Nevertheless, most studies have found higher rates of mental health visits per user in the fee-for-service sector (2).

In this paper we examine differences in the prevalence of psychiatric disorder and differences in the use of outpatient mental health services for adults enrolled in HMO or fee-for-service health insurance plans. Previous studies have had one or more important limitations, including lack of measures of specific psychiatric disorders, disregard for out-of-plan use, focus on only one HMO, and sampling based largely on subjects who were employed and thus had group coverage rather than on general populations. The National Institute of Mental Health (NIMH) Epidemiologic Catchment Area (ECA) study offered a unique opportunity to examine these issues while avoiding some of the limitations of previous studies. Specifically, we used ECA data on a household sample enrolled in various HMOs serving one of the geographic areas studied, and we used data on the prevalence of specific psychiatric disorders for both users and nonusers of outpatient mental health services.

METHOD

Sample

Data were obtained from the first phase of the Los Angeles ECA study. The design of the ECA program and the Los Angeles site have been described elsewhere (11, 12). The Los Angeles site consisted of two community mental health catchment areas. One was in East Los Angeles and the other was in West Los Angeles. The West Los Angeles area was predominantly (63%) non-Hispanic white and had a large number of private and public mental and general medical health care facilities in 1983, when the data were collected. The East Los Angeles area had a more stable and predominantly (83%) Hispanic population but had only a few mental and general medical care facilities.

Sampling consisted of a two-stage probability design. The completion rate for the survey was 69%, which is similar to response rates of other epidemiologic surveys conducted in Los Angeles (13), and the final sample consisted of 3,057 respondents.

Information on insurance coverage was obtained by using a 5-item battery. Responses were used to categorize individual respondents into five groups: Medicare enrollees, members of private fee-for-service plans, subjects in public-supported entitlement plans (Medicaid), members of an HMO, and the uninsured. A hierarchical system prevented overlap in these groups by placing an individual in only one group. If a person was a member of an HMO, then he or she was placed in that group only; after removing those respondents, enrollees in Medicare were placed in the Medicare group; next, the Medicaid group was made up; then the private group was formulated; finally, the remainder of respondents were placed in the uninsured group. Thus, the HMO group consisted of all respondents who were enrolled in an HMO plan (regardless of other coverage). The private group consisted of all those with private fee-for-service insurance unless they also had Medicare or were enrolled in an HMO; no respondents had both Medicaid and private fee-for-service insurance and no respondents had both HMO and private fee-for-service coverage.

In the present study the HMO and fee-for-service groups are the focus of the analysis. As a context, we also compared both groups with the group receiving Medicaid because of the known high prevalence of psychiatric disorder in that population (14–16).

Sources of Data

The presence or absence of psychiatric disorders was determined by using the NIMH Diagnostic Interview Schedule (DIS) (17). A Spanish language version (18) was available for those whose primary language was Spanish. Information obtained was used to generate psychiatric diagnoses comparable to those in *DSM-III*. All diagnoses reported here are those present in the 6 months preceding the interview, which was conducted in 1983.

Although the DIS identifies a large number of psychiatric disorders, not all diagnoses listed in *DSM-III* are covered by the instrument. The disorders identified differ in their severity (i.e., impact on functioning or presence of psychotic symptoms) and in the potential for response to treatment. Because we were particularly interested in examining differences in prevalence of serious and highly treatable disorders, before we analyzed the data we developed an indicator of having any such serious disorder among those assigned by the DIS. We categorized schizophrenic disorders, all affective disorders, alcohol and substance abuse, obsessive-compulsive disorder, and panic disorder as serious and treatable disorders. We excluded antisocial personality disorder, cognitive impairment, and phobia. Although we recognize that phobias can be both serious and treatable, many of the common phobias identified in a general population by the DIS may be mild. Because previous reports from the ECA have used a summary

TABLE 1. Demographic Characteristics of a Community Sample of Subjects With Private, HMO, or Medicaid Health Care Coverage

	Age (years)		Female		Employed		<12 Years of Education		Good-to-Excellent Health		Hispanic	
Coverage	Mean	SE	%	SE	%	SE	%	SE	%	SE	%	SE
Private (N=1,400)	37	0.9	49	1.2	80	1.2	46	1.4	85	1.0	42	1.5
HMO (N=410)	39	1.8	52	2.3	79	2.0	52[a]	2.3	85	1.9	50[b]	2.6
Medicaid (N=221)	39	2.5	64[c]	3.8	27[c]	2.9	79[c]	2.7	60[c]	4.1	68[c]	3.2

[a] Significantly different from the subjects with private insurance ($t=2.2$, df=1,808, $p<0.05$).
[b] Significantly different from the subjects with private insurance ($t=2.7$, df=1,808, $p<0.01$).
[c] Significantly different from the subjects with private insurance ($t=3.8$, df=1,619, $p<0.001$).

TABLE 2. Prevalence of Psychiatric Disorders in a Community Sample of Subjects With Private, HMO, or Medicaid Health Care Coverage

	Patients With Serious Psychiatric Disorder		Patients With Any DIS Disorder	
Coverage	%	SE	%	SE
Private (N=1,400)	12	0.8	18	0.9
HMO (N=410)	11	1.5	14	1.9
Medicaid (N=221)	18[a]	2.9	29[b]	3.4

[a] Significantly different from those with private insurance ($t=2.0$, df=1,619, $p<0.05$).
[b] Significantly different from those with private insurance ($t=3.1$, df=1,619, $p<0.005$).

variable for any DIS psychiatric disorder, the findings for that variable were also analyzed and reported here as "any DIS disorder" to allow comparison with previous reports.

As an indicator of the severity of psychopathology among those with psychiatric disorder, we used scores on the Center for Epidemiologic Studies Depression Scale (CES-D Scale) (19). This scale is considered by some to be an indicator of general psychological distress rather than a discrete measure of depression (20).

We used the system of Shapiro et al. (21) to categorize the mental health services: 1) Specialty mental health resources were psychiatrists, psychologists, psychiatric social workers, mental health counselors, mental health centers, and drug treatment centers. 2) General medical resources were medical care practitioners and emergency rooms. 3) Other human service resources were clergy, family service agencies, crisis centers, spiritualists, and natural therapists.

Statistical Analysis

Data were weighted to account for differential sampling probabilities and adjusted for age and sex by using the fee-for-service group as reference. The utilization data were generated by using SESUDAAN, a computer program that estimates standard errors of proportions and means for complex sample surveys (22). After controlling for other factors, we estimated multiple logistic regression models to examine unique associations between type of insurance and either prevalence of psychiatric disorder or use of mental health services. In these models, insurance groups were set up as a dummy variable with the fee-for-service group as the reference group. The chi-square values obtained with the logistic regression model were corrected for the clustered sampling design by using values obtained from a survey regression program (23).

RESULTS

Demographic Data

Table 1 lists the demographic characteristics of the subjects with HMO, private fee-for-service, and Medicaid coverage. The private and HMO groups were very similar in their characteristics, although the HMO had a higher percentage of enrollees who had less than 12 years of education and a higher percentage of Hispanic enrollees. The Medicaid group had very different characteristics from the HMO and private groups in that it had a lower average level of education, a higher rate of unemployment, and a lower level of general health and included a larger proportion of Hispanic people.

Although the HMO group had a larger Hispanic population than the private group, most of these Hispanics were born in the United States. As an indicator of acculturation we looked at the percentage of Hispanic respondents whose primary language was Spanish. The private and HMO groups were similar; each included 5% who spoke primarily Spanish.

Prevalence of Psychiatric Disorder

Table 2 reports the proportion of subjects with a serious DIS-*DSM-III* psychiatric disorder and the percentage who had any DIS-*DSM-III* psychiatric disorder within the preceding 6 months. The proportion of subjects who had any DIS-*DSM-III* psychiatric disorder or serious psychiatric disorder within the preceding 6 months did not differ significantly between the HMO and private groups. When the effects of other factors (sex, age, ethnicity, employment, education, and physical health) were controlled for by using multiple logistic regression, the HMO and private groups still did not have significantly different rates of serious psychi-

TABLE 3. Health Care Sectors Used in a Community Sample of Patients With Serious Psychiatric Disorders and Private or HMO Health Care Coverage

	Private (N=181)		HMO (N=49)	
Sector	%	SE	%	SE
General medical	5.7	2.0	4.8	2.4
Specialty mental health	15.2	2.5	16.2	5.8
Human services	6.3	1.8	5.8	3.2
General medical or specialty	19.2	2.8	20.5	6.3

atric disorder (the adjusted chi-square for the HMO group was 0.10, df=1, p>0.10). The Medicaid group had the highest proportion with a serious psychiatric disorder of the three insurance groups. However, of all subjects with a serious psychiatric disorder, most (54%) were enrolled in either the private or HMO sector, while 10% were covered through Medicaid and the rest were covered by Medicare or uninsured.

Among the subjects with a serious psychiatric disorder, there was no significant difference in level of psychological distress as assessed by the CES-D Scale for those enrolled in HMO or fee-for-service plans. However, the Medicaid group had more psychological distress than subjects in those two groups combined. The percent of subjects with a score of 16 or more in the HMO and private groups combined was 26%, compared with 67% in the Medicaid subjects.

Utilization Data

Table 3 presents the use of outpatient mental health services by subjects with a serious psychiatric disorder. There was no significant difference in use of the general medical, specialty mental health, or human services sector for the subjects in the private or HMO groups.

Because previous research has indicated that Hispanic subjects are less likely to use mental health services than non-Hispanic whites (24) and because the HMO group had a higher percentage of Hispanics, it was important to compare utilization rates for the two ethnic groups. We found similar levels of use of outpatient mental health services under HMO and fee-for-service plans for both Hispanic and non-Hispanic subjects (not shown in the table).

When we controlled for factors known to have an effect on use of the specialty mental health sector (ethnicity, sex, age, employment, education, and physical health), using multiple logistic regression, we found no difference in the probability of using the specialty mental health sector for the private and HMO groups (the adjusted chi-square for the HMO group was 0.17, df=1, p>0.10).

Among subjects with a serious psychiatric disorder who used services, the HMO group had a significantly higher mean number of outpatient visits to the general medical sector for mental health care than the private group (6.5 versus 3.6) (t=2.6, df=11, p<0.03) but had a lower number of outpatient visits to the specialty mental health sector for mental health care (1.6 versus 10.3) (t=6.6, df=34, p<0.001). The overall number of outpatient mental health visits in HMOs was about 40% lower than that in the private group because the number of outpatient visits to the specialty mental health sector was smaller in the HMO group.

DISCUSSION

Data from the current study indicate that HMOs serve a demographic group which is similar to that served by the private fee-for-service sector, at least in the large metropolitan area surveyed for this study. HMO enrollees were more likely to be Hispanic, but they were born in the United States and appeared to be as acculturated as those Hispanics in the fee-for-service group. The present study does not support previous studies (25) indicating that HMO enrollees may be younger and more fully employed than private fee-for-service plan members. In fact, the HMO and fee-for-service enrollees had similar mean ages, and most were employed. One reason our conclusions may differ from those of previous studies is that we examined all HMO enrollees in a general population sample, but most previous studies examined enrollees in particular HMOs and fee-for-service plans.

Although our data are limited to one geographic site, we provide here the first estimates of rates of psychiatric disorder in community samples by type of insurance coverage. Some studies (26, 27) have indicated that HMOs enroll a less mentally ill population than the private fee-for-service sector, although the RAND Health Insurance Experiment (2) did not find a selection bias. The latter study, however, used a global scale of mental health rather than psychiatric diagnoses and was conducted at a single HMO.

The results of the present study, which used community data, indicate that HMO and fee-for-service plans treat very similar groups of the mentally ill in terms of proportion of enrollees with any DIS psychiatric disorder and any serious and treatable psychiatric disorder. Although further development of severity indicators is needed, our indicator (level of psychological distress) was similar among those with psychiatric disorder in the HMO and fee-for-service plans. Thus, averaged over all the HMOs in Los Angeles, there is no evidence for either favorable or adverse selection in terms of psychiatric status. These findings suggest that the HMO and private fee-for-service sectors have similar responsibilities for providing psychiatric care.

We also found that although Medicaid enrollees were more likely to have serious psychiatric disorders, the majority (54%) of all respondents with such disorders were enrolled in an HMO or fee-for-service plan, while 10% were Medicaid recipients. This emphasizes the importance of private sector care for psychiatric patients, from both policy and clinical perspectives. It further emphasizes the importance of identifying differences in access and treatment style within the private sector.

Most previous studies comparing HMO and fee-for-service enrollees have found differences in the pattern of utilization of mental health services for these groups. These studies suggest that the rate of use of inpatient mental health care in HMOs is less and that the probability of using outpatient mental health care is greater than or at least equal to that in the fee-for-service sector. HMOs have also been shown to have a different style of treating patients with mental illness by substituting less expensive provider types and modes of therapy (2, 27, 28).

The study reported here is consistent with the RAND Health Insurance Experiment (2) in that we found a similar probability of any outpatient mental health use over a short period of time but a lower rate (approximately 40%) of overall outpatient mental health visits in HMOs than in the fee-for-service sector for subjects with a serious psychiatric disorder. Although the HMOs relied relatively more on general medical providers for the mental health care of patients with serious psychiatric disorder, this difference was not enough to offset the much larger difference in use of mental health specialty care for those with a serious psychiatric disorder. The overall smaller rate of outpatient mental health visits but similar probability of any outpatient mental health care implies that patients with serious psychiatric disorder have similar access but incur lower outpatient costs in HMOs than in fee-for-service plans.

The difference in benefit levels among the various private plans may have had an effect on the utilization results. Enrollees in fee-for-service plans were asked if they had outpatient mental health benefits, but only 58% knew if they had benefits. We were thus unable to use these data to adjust our findings. However, all HMO plans represented in this study had at least 20 outpatient mental health benefits per year, and a 1983 survey (29) found that 94% of the subjects with fee-for-service insurance had some outpatient mental health benefits.

From the present data we cannot determine whether the different style of care in HMOs resulted in greater morbidity or poorer quality of care among patients with serious psychiatric disorder. Further studies measuring morbidity and quality of care are needed to answer that question. By using cross-sectional data we were not able to delineate the effects of treatment differences. For example, if previous psychiatric treatment was more effective in the HMOs, then utilization of specialty services might be less at a later specific point in time because those services were no longer needed. Cross-sectional data also cannot determine whether patients with severe psychiatric disorder are more likely to leave HMOs over time. Furthermore, although differences in rates of psychiatric disorder and use of mental health services between HMO and fee-for-service plan members in the general population can be determined through community data such as those presented here, an individual HMO may be more or less likely to exclude particular types of psychiatric patients or have a different utilization pattern.

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Reliability of a Standardized Mini-Mental State Examination Compared With the Traditional Mini-Mental State Examination

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Objective: The objective of this study was to compare the reliability of the Mini-Mental State Examination with that of a new Standardized Mini-Mental State Examination, which has expanded guidelines for administration and scoring. Method: The subjects were 32 stable elderly residents of a nursing home and 16 elderly residents of a chronic care hospital unit. Six raters administered the Folstein Mini-Mental State to 22 of these stable elderly subjects, and five raters administered the standardized version to 26 of these subjects. Each subject was tested on three different occasions 1 week apart. Each rater tested 4–6 subjects at the first and third weeks and 4–6 different subjects at the second week. The analytic technique used was one-way analysis of variance to estimate the interrater variance and the intrarater variance. Results: The intrarater variance on all occasions was reduced by 86% and the interrater variance was reduced by 76% when the Standardized Mini-Mental State was used; the reductions in variance were significant (p<0.003). The intraclass correlation for the Mini-Mental State was 0.69; for the standardized version it was 0.90. It took less time to administer the Standardized Mini-Mental State than the Mini-Mental State. Conclusions: The Standardized Mini-Mental State had better reliability than the Mini-Mental State in this study group. Although the improved reliability of the Standardized Mini-Mental State was achieved by reducing measurement noise, this advantage would likely occur in a broad spectrum of patients.

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Screening instruments for cognitive impairment are frequently used in the elderly (1–3). The Folstein Mini-Mental State is the most widely used instrument to measure cognitive impairment in the elderly (1). This instrument has gained wide acceptance and has been used to assess cognitive function in clinical and epidemiologic settings (1, 4–8).

The Mini-Mental State measures orientation to time and place, immediate recall, short-term memory, calculation, language, and constructive ability. The maximum Mini-Mental State score is 30. The guidelines for its administration are short, and the scores for each item are recorded on the test form itself.

The Mini-Mental State is widely used because of its ease of administration and scoring. A substantial volume of literature has now accumulated about its validity (1, 4, 5). However, because the guidelines for its use are brief, the interpretation and scoring of answers are broad and subjective and may vary from one individual to the next. Differences between individuals scoring the test may affect the reliability of its scores.

Some of the Mini-Mental State items must be changed to accommodate different settings such as clinics, hospitals, and the subjects' homes. When it is administered at home, the word "hospital" has to be changed to "place" and the term "floor" may be irrelevant. Scoring of the praxis item (interlocking 5-sided figures) and calculation is subjective, and an individual's performance is affected by education (5). Because there is no time limit suggested for any reply, one could wait seconds or minutes for an answer. It is also not clear how one should score near misses, e.g., when a subject gives the last day of the month when it is the first day of the next month or gives a date of the month that is wrong by 1 day.

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The Mini-Mental State may be improved by developing more precise guidelines for its execution. We have developed a standardized version of this test (the Standardized Mini-Mental State) with explicit detailed guidelines for its administration and scoring (available on request from the first author). These stricter instructions were developed to improve the reliability of the instrument.

The goal of this study was to examine the effects of imposing stricter guidelines for administration and scoring on the reliability of the Mini-Mental State. The interrater reliability and the intrarater reliability of the traditional Mini-Mental State were compared with those of the standardized version.

The hypothesis tested was that the stricter directions in the Standardized Mini-Mental State would improve the reliability of the instrument.

METHOD

The study group comprised 48 elderly people, 32 of whom were residents of a nursing home and 16 of whom were residents of a chronic care hospital unit. Fourteen of the subjects were men and 34 were women. Their age range was 60–95 years. They suffered from a variety of conditions, including Alzheimer's disease, stroke, arthritis, and osteoporosis. Twenty-two were given the Mini-Mental State and 26 were given the Standardized Mini-Mental State. Eight of the subjects given the Mini-Mental State and six of the subjects given the Standardized Mini-Mental State were men.

Subjects who were medically stable, without aphasia, and without hearing impairment were included in the study. Subjects with acute illnesses or those taking drugs affecting cognitive function were excluded. Subjects who could not understand English, those with behavior problems, and those who had previously received a Mini-Mental State examination were also excluded.

Eleven volunteer gerontology students administered the instruments. These raters were recruited from advertisements posted at a university. Six of the 11 raters were randomly assigned to administer the Mini-Mental State and five were randomly assigned to administer the Standardized Mini-Mental State. None of the raters had been exposed to the Mini-Mental State previously. All were given a 15-minute talk on the Mini-Mental State before they were randomly assigned to administer the Mini-Mental State or the Standardized Mini-Mental State.

Each subject was tested at weeks 1, 2, and 3. Each rater tested 4–6 subjects on two occasions and 4–6 different subjects once. All subjects were tested in the mornings (between 9:00 a.m. and 12:00 noon). If a subject developed any problems that may have affected his or her cognitive function, the assessment was postponed until the next visit (a week later). Raters recorded the time for each assessment and response of the subject to each question. The raters were asked not to discuss the assessments with their colleagues until the study was completed.

Each subject tested with the Mini-Mental State was asked to do serial 7s or, alternatively, to spell "world" backwards as stated on the test itself. Those subjects who were tested with the Standardized Mini-Mental State were asked to perform serial 7s during the test and to spell "world" backwards at the end. Total scores for the Standardized Mini-Mental State reported here do not include the score from the spelling task.

The assessment schedule was arranged so that the same rater assessed a patient at weeks 1 and 3 and a different rater assessed the patient at week 2. The variability between scores for any particular subject from week 1 to week 2 or from week 2 to week 3 represents the between-rater (interrater) variation, and the variability from week 1 to week 3 represents the within-rater (intrarater) variation. The analytic technique used was one-way analysis of variance (ANOVA) (9, pp. 167–170) to estimate the intrarater variance and the interrater variance. Direct comparisons between the variance components (both within and between observers) resulting from the Mini-Mental State and the Standardized Mini-Mental State were achieved by using the variance ratio (F) test (9, pp. 37–41). The intraclass correlation (9, pp. 184–185) was computed as a measure of overall reliability.

RESULTS

The mean±SD scores at weeks 1, 2, and 3 for subjects given the Mini-Mental State were 17.71±8.49, 19.8±8.09, and 20.11±7.25. The scores for those given the Standardized Mini-Mental State were 25±4.54, 23.50±6.67, and 24.50±6.20 The mean differences over time were small, and formal statistical comparison with two-way ANOVA indicated nonsignificant Time differences for both the Mini-Mental State (F=1.66, df=2, 32, p=0.21) and the Standardized Mini-Mental State (F=1.61, df=2, 50, p=0.21).

Since there were no consistent changes over time, the variability of scores among the three measures for any subject represents the inherent test-retest reproducibility of the instrument when administered by different raters (week 1 versus week 2 and week 2 versus week 3) or by the same rater on two different occasions (week 1 versus week 3).

The simplest measure of the level of reproducibility is the within-subject standard deviation—the variation in a series of scores from the same subject. If these scores were all derived from the same rater we would expect the variation (standard deviation) to be smaller than if a different rater was used to test the subject on each occasion. Similarly, if one form of the test, say the Standardized Mini-Mental State, was more reproducible than the other, it would have lower within-subject standard deviations, both in the situation where the

TABLE 1. Within-Subject Standard Variations (Reproducibility) and Intraclass Correlations for the Mini-Mental State and the Standardized Mini-Mental State

Item	Same Raters, Week 1 Versus Week 3	Different Raters: Week 1 Versus Week 2	Different Raters: Week 2 Versus Week 3
Within-subject standard variation			
Mini-Mental State	4.8	4.8	3.9
Standardized Mini-Mental State	1.8	2.1	2.1
Reduction (%)	63[a]	55[b]	45[c]
Intraclass correlation			
Mini-Mental State	0.69	0.69	0.78
Standardized Mini-Mental State	0.92	0.90	0.89
Increase (%)	33	30	14

[a] $F=7.2$, $df=20, 26$, $p<0.0001$.
[b] $F=50$, $df=21, 26$, $p<0.0001$.
[c] $F=3.3$, $df=19, 26$, $p=0.003$.

same rater was used and when different raters were used.

The pooled within-subject standard deviation was estimated by using one-way ANOVA separately for the situation when the same rater or different raters were involved and separately for the Mini-Mental State and the Standardized Mini-Mental State. For example, the Mini-Mental State was administered to 18 subjects at week 1 and week 3 by the same raters. One-way ANOVA with Subjects as the grouping factor yields a pooled within-subject standard deviation of 4.8 (see table 1). The equivalent data for the Standardized Mini-Mental State yield a within-subject standard deviation of only 1.8, indicating that the Standardized Mini-Mental State had better reproducibility. A comparison of these two standard deviations (i.e., the corresponding variances) by an F test indicates a highly significant difference in reproducibility between the two tests (see table 1).

The Standardized Mini-Mental State Examination had significantly lower within-subject standard deviation for all comparisons in table 1, both when the same rater was involved and when different raters assessed the subjects (see table 1).

The distribution of scores did not affect the reliability of the Standardized Mini-Mental State. The main reason the Standardized Mini-Mental State was more reliable was because it reduced the intrarater variance. We stratified subjects into those with low (21 or less) and high (more than 21) scores to examine the effect of the value of the scores on reliability. The within-subject standard deviations of the higher-scoring group were 3.0 for the Mini-Mental State and 1.7 for the Standardized Mini-Mental State. The within-subject standard deviations for the lower-scoring group were 4.4 for the Mini-Mental State and 2.0 for the Standardized Mini-Mental State. Within each group the within-subject deviation was almost halved for the standardized version of the test.

Within-subject standard deviations represent the inherent "noise" associated with the measurement of cognitive function. Whether the noise is acceptable in terms of an instrument's performance depends on the strength of the "signal" we wish to detect with the test. The term "reliability" is used to describe an instrument's ability to distinguish differences between subjects and is analogous to a signal-to-noise ratio. The most usually quoted measure of reliability is the intraclass correlation, which is the proportion of the total variance that comprises the between-subject differences as opposed to measurement error.

The intraclass correlation for the same rater assessing a subject increased from 0.69 for the Mini-Mental State to 0.92 with the Standardized Mini-Mental State. Similar improvements in intraclass correlation were seen with the Standardized Mini-Mental State even when different raters were involved (see table 1).

The mean time required for each interview with the Mini-Mental State was 13.39 minutes, which was significantly greater than that required for the Standardized Mini-Mental State (10.47 minutes) ($t=2.92$, $df=124$, $p=0.004$).

The mean scores for spelling "world" backwards and serial 7s for 25 of the subjects who were given the Standardized Mini-Mental State were 3.88 ± 1.43 and 2.36 ± 1.61, respectively. This difference was statistically significant ($t=3.820$, $df=24$, $p<0.001$).

DISCUSSION

These findings show that the Standardized Mini-Mental State is more reliable than the Mini-Mental State. Different raters were used for both tests, and the assessments were done independently. This study design was used to determine interrater reliability and to avoid any contaminating effects of nonverbal communication between raters during simultaneous administrations.

There was no improvement in the scores obtained at weeks 1, 2, and 3 for both the Mini-Mental State and the Standardized Mini-Mental State, indicating no learning effect in the administration of the test three times in 3 weeks.

We compared the two tasks of spelling "world" backwards and calculating serial 7s in 25 of the subjects who were given the Standardized Mini-Mental State. The guidelines for administration of the Mini-Mental State suggest that these two tasks can be used alternatively to test attention and calculation. How to score the spelling of "world" backwards is not stated clearly in the Mini-Mental State. Since we could not obtain scores for both tasks in the Mini-Mental State, in this study we compared the two tasks only in the subjects tested with the Standardized Mini-Mental State.

All but two subjects scored less on serial 7s than on the spelling task. The difference in mean scores between these two items was statistically significant. For elderly patients who cannot spell "world" backwards, the alternative use of serial 7s may not be applicable because the task was more difficult and the elderly scored lower on this task. These two tests are not comparable. Although this finding is not generalizable to all elderly populations, further study needs to be done to resolve this issue.

It took less time to administer the Standardized Mini-Mental State than the Mini-Mental State. This may be due to the clearer guidelines for the administration, scoring, and timing of the responses in the Standardized Mini-Mental State. In the Mini-Mental State there are no clear guidelines or time limits, and the rater could wait a long time for an answer. In the Standardized Mini-Mental State we give reasonable time limits for answers, commensurate with the tasks, based on our experience with this instrument in clinical trials and in the day-to-day assessment of elderly patients with cognitive impairment (7, 8).

Providing a finite time helps the rater to limit the time taken to administer the instrument. Without these guidelines raters may have difficulty knowing how long they should wait for a response before they proceed to the next task. This may explain why the raters took longer to administer the Mini-Mental State.

We believe that the expanded guidelines in the Standardized Mini-Mental State make the Mini-Mental State easier to administer and increase the reliability of the instrument. However, some care should be exercised in interpreting our intraclass correlations. Although one might expect the measurement noise associated with cognitive function to be reasonably stable with different subgroups of geriatric subjects, the heterogeneity of these subgroups of subjects may vary markedly. This would affect the intraclass correlation in different subgroups.

This does not mean that the intraclass correlation is inappropriate as a measure of reliability, but it does suggest that the reliability of an instrument varies depending on the patient group in which it is being used. The intraclass correlations reported in this paper are typical for a chronic care-nursing home group. Although the improved reliability of the Standardized Mini-Mental State in this study was achieved by reducing measurement noise, we believe that this advantage would likely occur in a broad spectrum of patient groups.

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Neuropsychological Testing of Patients With Borderline Personality Disorder

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Objective and Method: This study examined whether a battery of neuropsychological tests could detect cognitive deficits—particularly in the areas of perception, learning, and memory—in patients with borderline personality disorder. The test battery was completed by 16 research outpatients with borderline personality disorder, typified by behavioral dyscontrol and diagnosed according to DSM-III-R *criteria and the Diagnostic Interview for Borderline Patients. A comparison group of 16 normal volunteers also completed the test battery. Results: The performance of the borderline patients was significantly impaired in comparison with that of the normal group on memory tests requiring uncued recall of complex, recently learned material. Cues given on an auditory memory task partially corrected that deficit. The patients' performance was also significantly impaired on several visual perceptual tests. These deficits do not appear to have been attributable to attentional problems, psychomotor impairment, current major depression, or history of alcohol abuse. Conclusions: The observed difficulties in separating essential from extraneous visual information and in recalling complex material may be relevant in understanding some of the clinical features of borderline personality disorder. The observed memory improvement resulting from cueing suggests specific strategies that may be used to aid patients' recall of complex material.*

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The clinical literature on borderline personality disorder is replete with examples of memory impairment and cognitive distortions occurring in psychotherapy and in daily life. Zetzel (1) emphasized the hysterical style characteristic of patients with borderline disorders, and Kroll (2) recently reemphasized histrionic features of borderline personality disorder, including a "tendency toward global perceptions with a loss of attention to details, distortion of the meaning of an event, patterns of confusion and spotty amnesias." In spite of these recurring observations, there has been little neuropsychological testing to examine whether these impairments can be demonstrated in an objective manner and, if so, whether they are attributable primarily to motivated defensive operations of the ego or to more fundamental problems with perception, cognition, and memory in borderline personality disorder.

The psychological testing literature thus far has focused on the "intact WAIS/disturbed Rorschach" pattern supposedly characteristic of borderline personality disorder, in which intact performance on structured psychological tests such as the WAIS contrasts with "psychotic" thinking on unstructured projective tests such as the Rorschach (3–6). A review of recent literature, however, suggests that there is only limited evidence to support the validity of this pattern (7, 8). Furthermore, testing limited to the WAIS and the Rorschach test leaves unaddressed a vast area of neuropsychological functioning in borderline personality disorder. To our knowledge, only one report of the administration of quantitative neuropsychological test batteries has been published (9). No cognitive deficits in borderline patients were found, but the use of historical norms rather than a normal comparison group clouds the interpretation of that study.

Through the administration of a comprehensive battery of neuropsychological tests and comparison with a group of normal volunteers, we sought to examine several broad questions. Could such a battery be used to identify cognitive disturbances in borderline personality disorder patients? In particular, could problems in the areas of perception, learning, and memory be identified? Is major depression or a history of alcohol abuse related to impaired performance in this population? How might any impairments relate to the clinical presentation of these patients?

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METHOD

Sixteen research outpatients with borderline personality disorder and 16 normal volunteers completed a battery of neuropsychological tests. The borderline patients had been referred by mental health professionals in the community and participated in a 3-week inpatient research program if they 1) met the *DSM-III-R* criteria for borderline personality disorder, verified by the Structured Interview for the DSM-III Personality Disorders (10, 11); 2) had a score of at least 7 on the Diagnostic Interview for Borderline Patients (12); 3) showed clear behavioral evidence of dyscontrol—suicide attempt, self-injury, violence toward persons or property, or any combination of these; 4) were in the age range of 18–45 years; 5) had no cardiovascular, renal, hepatic, or seizure disorder; and 6) had no history of drug or alcohol dependence according to *DSM-III-R* criteria within the past 2 years. Presence or absence of a current affective disorder according to *DSM-III-R* criteria was determined through clinical interviews conducted by one of the authors (D.L.G.) and one of two other staff psychiatrists at the National Institute of Mental Health. Past alcohol abuse was also rated according to *DSM-III-R* criteria by using self-reports and record review. No subject had a history of drug dependence or abuse. All medications were withdrawn from the patients at least 2 weeks before admission to the study.

Sixteen healthy volunteers were recruited through advertisement and through the National Institutes of Health normal volunteer office. All were screened by means of clinical interviews. The gender composition of the patient group and the normal volunteer group was identical (13 female and three male subjects in each). There was no significant difference in age between the groups: for the borderline patients, mean±SD=29.4±7.3 years, range=20–41; for the normal subjects, 27.5±6.4 years, range=21–45 ($t=-0.78$, df=30, n.s., two-tailed test). All patients and normal volunteers had completed at least 12 years of education; the mean±SD was 15.1±2.1 years for the patients and 15.5±2.4 years for the normal comparison subjects ($t=0.54$, df=30, n.s., two-tailed test). All of the normal volunteers were without histories of psychiatric disorders, neurological disorders, and drug and alcohol abuse and denied recent use of both prescription medication and illicit drugs. None had a family history of psychiatric disorders in first-degree relatives. Parental and sibling history was not obtainable for one volunteer who had been adopted as an infant. Written informed consent was obtained from all patients and normal volunteers.

The test battery was designed to assess several categories of cognitive functioning: general intelligence, problem solving, and hypothesis formation; simple and complex visual and auditory memory; filtering of complex visual stimuli; and general psychomotor performance. All tests used are listed in table 1. A single examiner (K.M.O.) administered all tests, using standard methods except where noted later in the paper.

Because a number of dependent variables were not distributed in a normal fashion, group differences were analyzed with the Wilcoxon rank sums test (see table 1). A stepwise discriminant function analysis and a subsequent classification analysis with a jackknife procedure were performed to identify a core group of variables with relatively independent power to discriminate between the borderline and normal groups.

RESULTS

The mean WAIS-R (13) full-scale IQs and verbal IQs in both groups were in the high average range and were not significantly different. Performance IQ was significantly lower in the borderline personality disorder group (see table 1). This difference was attributable primarily to a highly significant difference on the digit symbol subtest, a coding test that assesses psychomotor performance and visual discrimination and filtering. The Wisconsin Card Sorting Test (14), which assesses hypothesis formation, problem solving, and the ability to shift set, did not discriminate between the patients and the normal volunteers.

On the Wechsler Memory Scale (15) logical memory (story recall) subtest, in which subjects were asked to remember stories they had been told by the examiner, both immediate and delayed recall of story elements was lower in the borderline personality disorder group (table 1). Following delayed recall, subjects were given cues to aid the recall of story elements not previously remembered. Cueing produced a significantly greater number of additional story elements recalled in the borderline group; after cues, there was no significant difference between groups. Borderline patients demonstrated no impairment on other Wechsler Memory Scale subtests, which assess memory for simple visual and auditory items. Nor did they show impairment on the Seashore tests (16), which assess perception and memory of nonverbal auditory tones.

On the Rey-Osterrieth test (17, 18), which involves copying and then drawing from memory a complex visual figure, the copy score of the patients with borderline personality disorder was almost identical to that of the normal volunteers, but the patients' scores were significantly lower on recall after 5 minutes and delayed recall after 45 minutes (table 1). This suggests intact visuoperceptual and visuomotor skills but impaired complex visual memory. On the Corsi Blocks (19), which is a visual analogue of the WAIS-R digit span subtest and requires the subject to remember and point out increasingly long patterns of three-dimensional blocks on a board, the performance of the borderline personality disorder patients was significantly impaired on both the forward and backward tests.

On the Embedded Figures Test (20), which requires subjects to remember a simple geometric shape they are shown and then use visual discrimination and fil-

TABLE 1. Neuropsychological Test Scores of 16 Borderline Personality Disorder Patients and 16 Normal Comparison Subjects

	Normal Subjects		Borderline Patients		p Value <0.10[a]
Neuropsychological Test	Mean	SD	Mean	SD	
General intelligence and problem solving					
WAIS-R					
Information	12.13	2.75	12.75	1.65	—
Digit span	12.38	2.80	11.75	2.52	—
Vocabulary	13.06	2.79	14.00	2.53	—
Arithmetic	11.31	2.35	10.69	2.36	—
Comprehension	13.06	2.46	12.88	2.87	—
Similarities	12.44	2.58	12.06	1.98	—
Picture completion	11.63	1.93	11.63	2.33	—
Picture arrangement	12.38	2.75	10.88	2.85	—
Block design	10.88	1.96	10.94	2.08	—
Object assembly	10.75	2.11	10.00	1.86	—
Digit symbol	13.19	2.10	10.75	1.73	<0.002
Verbal IQ	115.50	14.48	114.88	10.61	—
Performance IQ	112.81	9.44	104.75	11.72	<0.04
Full-scale IQ	116.44	13.23	111.75	11.24	—
Wisconsin Card Sorting Test					
Categories achieved	6.00	0.00	5.88	0.50	—
Perseverative errors	7.25	3.45	8.75	6.42	—
Nonperseverative errors	5.25	3.51	8.13	6.57	—
Trials to first category	12.44	3.69	15.06	7.28	—
Unique responses	0.25	0.77	0.50	0.89	—
Failure to maintain set	0.69	1.14	0.63	1.02	—
Memory					
Wechsler Memory Scale					
Logical memory (stories)	12.81	2.53	10.42	3.62	<0.03
Delayed logical memory	10.72	2.35	8.67	2.75	<0.03
Improvement from cues	2.56	1.55	4.19	1.72	<0.01
Logical memory with cues	11.92	2.49	10.69	2.89	—
Visual reproduction	12.56	1.03	11.25	2.89	—
Associate learning	19.00	1.59	18.56	2.13	—
Delayed associate learning	6.63	0.50	6.66	0.70	—
Digits forward	7.75	1.84	7.06	1.29	—
Digits backward	6.63	1.41	5.88	1.15	<0.08
Memory quotient	125.88	11.80	118.56	12.10	<0.08
Seashore tests					
Rhythm	26.93	2.25	26.31	2.82	—
Tonal memory	25.73	4.35	23.06	5.32	—
Rey-Osterrieth test					
Copy	34.75	1.48	33.50	2.71	—
Copy time	275.36	156.62	253.73	109.15	—
Recall	25.97	5.02	18.81	7.53	<0.02
Delayed recall	26.06	4.73	20.30	6.85	<0.03
Visual perception					
Corsi Blocks					
Forward	6.75	1.18	5.81	0.98	<0.02
Backward	6.06	0.93	5.38	1.15	<0.05
Embedded Figures Test					
Score	35.06	21.60	70.94	41.87	<0.003
Number of failures	0.69	1.01	2.88	3.16	<0.002
Road-map Test					
Number of errors	1.13	1.82	2.00	2.90	—
Time (sec)	97.75	18.05	127.56	46.74	<0.02
Facial Memory Test	24.69	3.28	23.31	4.81	—
Verbal Incidental Learning Test					
Free recall	8.67	2.61	8.47	2.92	—
Recognition memory	29.00	1.46	28.40	1.55	—
Visual Search and Neglect Test					
Number of errors	0.00	0.00	0.31	1.01	—
Number of omissions	2.00	4.00	1.50	1.71	—
Time (sec)	121.13	37.04	139.94	41.35	—
Street Gestalt Completion Test	9.81	1.51	10.13	1.54	—

[a] All group differences were analyzed with the Wilcoxon rank sums test.

tering to identify the shape within a more complex one, the borderline patients' performance was impaired, as indicated by both the mean score and the number of failures, a measure we had added (table 1).

On Money's Standardized Road-map Test of Direction Sense (21), which assesses spatial orientation and visual discrimination and filtering by requiring the subject to describe turns in the path the examiner is tracing among a grid of lines, there was no difference between groups on errors, but the borderline patients were significantly slower on the time measure, which we had added. There were no significant group differences on four other visual perception tests: the Facial Memory Test, the Verbal Incidental Learning Test, the Visual Search and Neglect Test (all designed by P.B.), and the Street Gestalt Completion Test (22).

On the tests in which there were significant differences between the borderline personality disorder group and the normal comparison subjects, we examined the possible role of major depression and history of alcohol abuse within the borderline group by comparing the scores of the borderline patients who had each characteristic with the scores of the borderline patients who did not have each characteristic. Neither current major depression (N=7, none with melancholia) nor a history of alcohol abuse (N=6) was significantly associated with lowered performance on any of the items that discriminate borderline personality disorder patients from normal subjects.

A stepwise discriminant function analysis was performed to identify the variables with the greatest independent power to discriminate between the borderline patients and the normal comparison group. After entry of the most powerful single discriminator, the WAIS-R digit symbol subtest score ($R^2=0.31$, F=13.0, df=1, 29, $p<0.002$), two additional variables that were almost equally powerful independent discriminators were identified: the Rey-Osterrieth recall score (partial $R^2=0.19$, F=6.7, df=1, 28, $p<0.02$) and the improvement from cues score on the Wechsler story recall (partial $R^2=0.19$, F=6.5, df=1, 28, $p<0.02$). Each of these two variables remained a powerful discriminator after entry of the other into the discriminant function, and no fourth variable contributed significant power to the discriminant function. The three discriminator variables were then used in a series of discriminant function classification analyses with a jackknife procedure; this resulted in the correct classification of 87.5% (N=28) of the 32 subjects.

DISCUSSION

This group of patients with borderline personality disorder demonstrated significant deficits on the Wechsler Memory Scale story recall, on recall of the Rey-Osterrieth figures, on the Embedded Figures Test, on the Corsi Blocks, on the Road-map Test, and on the WAIS-R digit symbol subtest. Two major dimensions of neuropsychological functioning were identified in these discriminating items: memory and the process of visual discrimination and filtering.

The observed memory deficits seem to be partly a factor of the complexity of the material. The performance of the borderline patients was equivalent to that of the normal volunteers on a simple visual memory task (Wechsler visual reproduction) and a simple auditory memory task (Wechsler associate learning) but was impaired on a complex visual memory task (Rey-Osterrieth) and on a complex auditory memory task (Wechsler story recall, immediate and delayed). Apparent memory deficits can result from problems with initial learning, retention, or recall of the material. Our patients had difficulty with spontaneous recall of complex stories. However, when cues to the "forgotten" story elements were provided (e.g., "Do you remember where the robbery took place?"), the patients' performance approached that of the normal subjects. This pattern suggests that the problem may lie less in an initial learning deficit and more in recalling learned material without cues.

Contrary to clinical anecdotal reports of the difficulties borderline personality disorder patients experience in retaining even a visual representation of their therapists in their minds, the performance of these borderline patients was not impaired on the Facial Memory Test. However, this test is not affect-laden and does not assess true "evocative memory," the ability to summon images from within that is reportedly deficient in borderline personality disorder (23), since the subject is only required to recognize the correct faces among a larger series of faces.

Clinicians commonly observe that patients with borderline personality disorder have difficulty remembering past experiences, including previous therapy sessions. This difficulty with recall is often felt to be defensive in nature. Our preliminary results suggest that the memory difficulties experienced by borderline patients may not be confined to emotion-laden, conflictual material but may represent a broader deficit in remembering complex material. Such memory deficits might contribute to the difficulties borderline patients experience in maintaining a continuous sense of self and in using the past to respond to present events and predict future consequences.

Therapists may find that encouraging patients' use of self-ratings, diaries, and other concrete aids to memory can facilitate recall, much as patients' use of transitional objects may cue evocative memory. Our tentative results also suggest that verbal cueing may assist in the recall of "forgotten" material (e.g., "Do you remember that when this happened before, you felt . . . ?").

The borderline personality disorder patients also experienced significant difficulty on four tests requiring what we call visual filtering and discrimination, i.e., filtering out extraneous stimuli and selecting relevant visual details from a complex field. Impaired performance on two of these (the Embedded Figures Test and the Corsi Blocks) might be attributable to the tests' memory components, but impaired performance on the WAIS-R digit symbol subtest and on the Road-map Test suggests a problem independent of memory difficulties.

In contrast to these results, the borderline patients did not have difficulty with elaborating an incomplete drawing on the Street Gestalt Completion Test or in organizing elements into a whole, as on the WAIS-R object assembly and block design subtests.

The apparent difficulties with visual discrimination and filtering in borderline personality disorder can be conceptualized in several intriguing ways. Witkin, who originated the Embedded Figures Test, felt that poor performance on this test reflects strong field dependency, in which perceptions of individual details are strongly influenced by the surrounding context (19). He believed that strong field dependency tends to be associated with poor psychological differentiation. The difficulties of borderline patients in observing and recalling details of a complex figure or story also suggest a hysterical cognitive style, consistent with clinical descriptions of the borderline cognitive style and with the classification of borderline personality disorder in the dramatic cluster of personality disorders.

Since many neuropsychological tests inherently assess attention, motivation, and psychomotor performance, we examined these factors in relation to the pattern of impairment in borderline personality disorder. The Visual Search and Neglect Test, which requires high attention, sustained motivation, and psychomotor performance on a simple task, showed no group difference between the borderline patients and the normal volunteers. Of the three WAIS-R subtests that have a considerable attentional component (digit span, arithmetic, and digit symbol), only the digit symbol subtest showed a significant difference between the groups. Similarly, of the four WAIS-R performance subtests with a psychomotor component (object assembly, block design, picture arrangement, and digit symbol), again only the digit symbol subtest showed a group difference. The lower scores on recall in the Rey-Osterrieth test were not attributable to psychomotor skills, since there was no significant difference between the patients and the normal subjects in copy score. Finally, an analysis of the effects of major depression and prior alcohol abuse suggested that these factors did not account for the observed deficits in the borderline personality disorder patients' performance.

Any small-scale study using an extensive battery of tests must be regarded as exploratory. Although the number of significant differences we observed (12 of 49) far exceeds that expected on the basis of chance alone, and the differences appear to form a meaningful pattern, the results must be replicated before conclusions are drawn about neuropsychological functioning in borderline personality disorder.

These results may not be typical of all patients with borderline personality disorder according to the *DSM-III-R* criteria. Although our borderline subjects had long-standing, firmly established diagnoses, they were characterized by particularly prominent behavioral dyscontrol. They were also of above-average intelligence, able to cooperate with an extensive program of research, and able to tolerate being medication free for several weeks. Patients with recent alcohol/drug dependence were excluded from the study, and the subgroup of depressed borderline patients included no melancholic patients.

Our preliminary results suggest several questions for future research. Are the observed memory deficits due to impaired encoding, impaired retrieval, or both functions? Are memory difficulties more prominent with affect-laden material? Will neuropsychological testing suggest any specific anatomical regions of interest? For example, we observed poor performance on tasks that may be particularly sensitive to impairment in both the dominant temporal lobe (Wechsler Memory Scale logical memory subtest) and the nondominant temporal lobe (Rey-Osterrieth test, Embedded Figures Test, Corsi Blocks).

Ultimately, confirmation of specific neuropsychological abnormalities in some patients with borderline personality disorder may have important implications for clinical work with these patients. It is therapeutically valuable to know that some borderline patients may have genuine impairment in filtering information and recalling complex material, in addition to their "motivated" forgetting and defensive cognitive styles. It is additionally useful for clinicians to know that cueing can help in the retrieval of material. While no one would suggest that neuropsychological deficits are the cause of this complex personality disorder, deficits in visual perception and in retrieval from memory may contribute to the cognitive difficulties observed in borderline personality disorder.

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A Family-Genetic Study of Girls With *DSM-III* Attention Deficit Disorder

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Objective: The authors evaluated family-genetic risk factors in girls with attention deficit disorder and compared these results to findings in the authors' previous study of boys with attention deficit disorder. Method: Twenty-one girls with attention deficit disorder and 20 normal comparison girls were consecutively ascertained from a pool of existing and new referrals from a pediatric psychopharmacology unit and a medical pediatric unit of the same urban hospital. First-degree relatives of the attention deficit disordered girls (N=69) and of the normal girls (N=71) were also assessed. Both groups of girls and their relatives were evaluated on the basis of structured diagnostic interviews conducted by raters who were blind to the clinical status of the probands. Results: The relatives of the girls with attention deficit disorder had higher risks for attention deficit disorder, antisocial disorders, major depression, and anxiety disorders. The higher risk for attention deficit disorder could not be accounted for by gender or generation of relative, age of proband, social class, or family intactness. These findings are highly consistent with the findings in the authors' previous study of boys with attention deficit disorder, which was conducted with identical methods. Conclusions: This study provides further support for the validity of the diagnosis of attention deficit disorder in girls and suggests that the genders share a common biological substrate.
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Attention deficit disorder is a highly prevalent heterogeneous disorder now estimated to affect 6% to 9% of school-age children (1, 2). Although two to nine times as prevalent in boys as in girls (1–3), it is nevertheless a noteworthy cause of psychiatric disability in girls. However, little is known about the syndrome in girls because most studies of attention deficit disorder have provided little or no information about females (4, 5). Although some reasons for the dearth of information about girls are unknown, the focus on boys has probably been due to their greater prevalence of the disorder and the desire of researchers to obtain homogeneous samples.

Overall ratings of psychopathology, personality, emotional functioning, and response to stimulants do not differentiate boys and girls with attention deficit disorder (5, 6). However, the available literature on girls with attention deficit disorder (7, 8) indicates that they have higher rates of cognitive impairment, depression, and low self-esteem and lower rates of severe behavioral disturbances than boys with the disorder. In addition, lower prevalences of maternal depression and marital discord have been found in the families of girls with attention deficit disorder than in the families of such boys (4). Because family disruption and severe behavioral disturbances are observed less frequently among girls than among boys with attention deficit disorder, they may be less likely to come to the attention of health care providers (3, 9). For example, girls with attention deficit disorder are also less likely than boys to receive stimulant treatment despite findings that their response to treatment may be the same (5). This underidentification and undertreatment of girls with attention deficit disorder may have substantial mental health and educational implications, suggesting that research is needed to develop a better understanding of clinical indicators of attention deficit disorder in girls.

Family-genetic studies have consistently found relatives of boys with attention deficit disorder or hyper-

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activity to be at greater risk for attention deficit disorder and other psychiatric disorders than relatives of boys without attention deficit disorder (10–16). The familial transmission of attention deficit disorder among families with a son who has the disorder provides external validation for the diagnosis in boys and suggests genetic influences in the disorder. The extension of these findings to girls would provide further support for the validity of the attention deficit disorder diagnosis in girls and suggest that the genders have a common biological substrate. In this report we examine familial risk factors in girls with attention deficit disorder and in normal comparison girls and compare these results to our previously published data on boys with attention deficit disorder (11).

METHOD

This study was an extension of a previously reported study of 73 boys with attention deficit disorder, which was conducted with identical methods (11). The 21 girls with attention deficit disorder were Caucasian, non-Hispanic, nonadopted 6–17-year-old outpatients, consecutively ascertained from the pool of existing and new referrals to a pediatric psychopharmacology unit and a medical pediatric clinic of an urban hospital. All but one of the girls with attention deficit disorder met the clinical criteria for the diagnosis of attention deficit disorder with hyperactivity according to *DSM-III*; the other one met the criteria for attention deficit disorder without hyperactivity. These girls had severe symptoms that resulted in their referral to a specialized psychopharmacology clinic. Clinical diagnosis was based on clinical interviews with the child and family by child psychiatrists. The symptoms reported were manifested both at home and in school. The clinical diagnosis of attention deficit disorder was also confirmed by a structured psychiatric interview with the mother by a trained rater; the interview used was the Diagnostic Interview for Children and Adolescents—Parent Version (DICA-P) (17, 18). Although clinically all but one of the girls met the *DSM-III* criteria for attention deficit disorder with hyperactivity, the diagnostic confirmation with the DICA-P did not permit the differentiation of attention deficit disorder with and without hyperactivity. The 20 normal comparison girls were referred from the pediatric primary care service of the same hospital. They were screened for absence of medical and psychiatric disorders by asking the parent or the pediatrician if the child had any known medical or psychiatric problem.

The probands and all available first-degree biological relatives were evaluated through structured diagnostic interviews by raters who were blind with respect to the clinical status of the probands; 69 relatives of the girls with attention deficit disorder and 71 relatives of the normal girls were interviewed. The psychiatric assessments of the probands and their siblings were also based on the DICA-P interviews with the mothers. The diagnostic assessments of the parents were based on a direct interview with each parent, in which the rater used the National Institute of Mental Health Diagnostic Interview Schedule (DIS) (19, 20) to cover adult disorders and an addendum based on the DICA-P to cover childhood disorders. A diagnosis was considered positive if, based on the interview results, the *DSM-III* criteria were unequivocally met. Like Costello et al. (21) and Milich et al. (22), we did not differentiate between aggressive and nonaggressive conduct disorders. Since the structured interviews generate diagnostic information about both past and current disturbances, the rates of illness reported here are lifetime prevalences.

The interviews were conducted by four trained raters with undergraduate degrees in psychology, and interrater reliability was established. The training consisted of familiarization with the study design and objectives, *DSM-III*, and the DICA-P and DIS. During training the raters first observed interviews carried out by experienced raters and clinicians and subsequently conducted at least two interviews while observed by senior raters before starting to rate independently. The raters were supervised by one of us (J.B.). The interviews were audiotaped for random review and reliability assessments. The kappa coefficients of agreement among raters were greater than 0.95 for the diagnoses of children and adults with the exception of major depression in adults (kappa=0.83).

Since many of the psychiatric disorders examined in this study have a variable age at onset, the observed rate of illness in relatives had to be corrected for the fact that many of the relatives had not lived through the entire period of risk. For example, if we assume that onset of major depression usually occurs before age 65 but is subsequently unlikely, then a well 30-year-old has not lived through the period of risk, whereas a well 70-year-old has survived the risk period. Thus, our estimates of risk had to be adjusted so that the degree to which a well individual was counted as healthy increased with the individual's age at the evaluation. The Kaplan-Meier estimate from survival analysis (23) provides a suitable method for age adjustment (24). Age-corrected rates of illness are usually called morbidity risks, a convention that is adhered to in this report. We made group comparisons of morbidity risk estimates with z tests using standard errors of the Kaplan-Meier estimates computed with Greenwood's formula (25). A chi-square test from the proportional hazards model was used to determine whether the effect of proband diagnosis on illness in the relative remained after statistically controlling for other variables. This was accomplished by blocking the proportional hazards analysis predicting relative illness from proband diagnosis by strata formed from the third variable. The Kruskal-Wallis test was used for continuous variables. All analyses were two-tailed.

TABLE 1. Sociodemographic Characteristics of 21 Girls With Attention Deficit Disorder, 20 Normal Girls, and 73 Boys With Attention Deficit Disorder

	Girls With Attention Deficit Disorder		Normal Girls		Boys With Attention Deficit Disorder[a]	
Characteristic	Mean	SD	Mean	SD	Mean	SD
Age (years)	9.2	2.9	10.4	5.0	10.6	3.2
Socioeconomic status (1 to 5)	2.6	1.3	3.1	0.8	3.2	1.2
Age of parents (years)	37.3	4.9	38.1	5.5	38.5	6.5
Age of siblings (years)	9.6[b]	5.5	10.5	4.2	12.9	6.1
Number of brothers	0.7	0.8	0.6	0.7	0.8	0.8
Number of sisters	1.0	0.9	1.1	0.4	0.8	0.7

[a] As reported elsewhere (11).

[b] Significantly different from age of siblings of boys with attention deficit disorder (χ^2=6.8, df=1, p=0.009, Kruskal-Wallis test).

RESULTS

Girls With and Without Attention Deficit Disorder

The sociodemographic characteristics of the three groups are displayed in table 1. The girls with attention deficit disorder and the normal girls did not significantly differ in socioeconomic status, number of brothers, number of sisters, age, age of parents, or age of siblings (p>0.05 for each Kruskal-Wallis test). The percentage of mothers who were interviewed was 90.0% for the girls with attention deficit disorder (18 of 20), 100.0% for the normal girls (N=20), and 98.6% for the boys with attention deficit disorder (N=72). The proportions of fathers interviewed were only 77.8% (14 of 18), 75.0% (N=15), and 78.1% (N=57), respectively, but they did not differ significantly between groups. Separated or divorced parents were more common among the girls with attention deficit disorder (35.0%, 7 of 20) than among the normal girls (5.0%, N=1) (p=0.04, Fisher's exact test). In other comparisons of the girls with attention deficit disorder and the normal girls (Fisher's exact test), the following significant differences were found: major depression, eight girls (38.1%) versus none, respectively (p=0.002); oppositional disorder, 15 (71.4%) versus none (p<0.001); phobias, 10 (47.6%) versus none (p<0.001); and school dysfunction, 13 (61.9%) versus five (25.0%) (p=0.03). Although the rate of conduct disorder was higher among the girls with attention deficit disorder (19.0%, N=4) than among the normal girls (N=0), the difference did not attain significance (p=0.11).

As indicated in table 2, the morbidity risk for attention deficit disorder among the relatives of the girls with that diagnosis was significantly higher than that among the relatives of the normal girls (z=2.8, p=0.005). The relatives of the girls with attention deficit disorder also had higher risks for one or more antisocial disorders (z=2.7, p=0.006), major depression (z=3.0, p=0.002), and anxiety disorders (z=2.9, p=0.004). The effect for antisocial disorders was accounted for primarily by the girls with attention deficit disorder and comorbid oppositional disorder (z=3.2, p=0.002). Three anxiety disorders were more prominent among the relatives of the girls with attention deficit disorder: overanxious disorder (z=2.7, p=0.007), panic disorder (z=2.1, p=0.04), and phobic disorders (z=2.3, p=0.02). Their relatives were also more likely to have required extra help in school (z=2.8, p=0.004) and to have been placed in special classes (z=2.1, p=0.04) than the relatives of normal girls.

After controlling for gender of relative (χ^2=8.8, df=1, p=0.003) and for generation (parent and sibling) of relative (χ^2=8.0, df=1, p=0.005), the risk for attention deficit disorder among the relatives of the girls with this disorder remained significantly greater than the risk among the relatives of the girls without the disorder. Further examination of the differences in risk for attention deficit disorder by gender of relative revealed that male relatives of both groups of girls had a higher risk for substance use disorders than female relatives (25.2% versus 6.2%; z=2.3, p=0.02) and a lower risk for affective disorders (1.4% versus 16.6%; z=2.6, p=0.01).

Social class (1=highest, 5=lowest) and family intactness (divorced or separated versus intact family) were used as basic indicators of the quality of the psychosocial environment. The greater familial risk for attention deficit disorder in the relatives of the girls with attention deficit disorder remained significant after controlling for intactness of family (χ^2=8.2, df=1, p=0.004). Similarly, the association between attention deficit disorder in probands and relatives was maintained when socioeconomic status was controlled for (χ^2=8.8, df=1, p=0.003). Consistent with these findings, the morbidity risk for attention deficit disorder did not differ significantly between intact and broken families (17.4% versus 10.9%; p=0.44) or between families with high, middle, and low social class (16.0%, 7.2%, and 12.3%; p>0.10 in each comparison).

Girls and Boys With Attention Deficit Disorder

As shown in table 1, the girls and boys with attention deficit disorder did not significantly differ in socioeconomic status, number of brothers, number of sisters, age of proband, or age of parents (p>0.05 for each Kruskal-Wallis test); the percentages of intact families were also similar: 65.0% (N=14) and 63.0% (N=46). However, the siblings of the boys were significantly older than the siblings of the girls. The girls had a higher rate of phobia than the boys, 47.6% (N=10) versus 16.4% (N=12) (p=0.007, Fisher's exact test). Although the two groups did not significantly differ in rates of other comorbid psychiatric disorders, the girls had a lower prevalence of conduct disorder (19.0% [N=4] versus 32.9% [N=24]; p=0.29) and a higher rate of major depression (38.1% [N=8] versus 26.0% [N=19]; p=0.29).

Although there was no statistically significant difference in the risk for attention deficit disorder in the

TABLE 2. Morbidity Risk of Psychiatric Disorders and School Dysfunction Among Relatives of 21 Girls With Attention Deficit Disorder, 20 Normal Girls, and 73 Boys With Attention Deficit Disorder[a]

	Morbidity Risk (%) in Relatives					
	Of Girls With Attention Deficit Disorder (N=69)		Of Normal Girls (N=71)		Of Boys With Attention Deficit Disorder (N=264)[b]	
Disorder	Risk	SE	Risk	SE	Risk	SE
DSM-III diagnoses						
Attention deficit disorder	19.5	4.9	4.3[c]	2.4	25.1	2.8
Antisocial disorders	17.0	5.1	2.0[c]	2.0	23.4	2.9
Conduct disorder (sibling)	3.1	3.1	0.0	0.0	6.9	3.3
Antisocial personality disorder (parent)	2.7	2.7	2.5	2.5	9.2	2.4
Oppositional disorder	15.0	4.7	0.0[c]	0.0	20.9	2.8
Affective disorders	17.2	5.7	0.0[c]	0.0	27.1	4.1
Major depression	17.2	5.7	0.0[c]	0.0	25.0	4.0
Dysthymic disorder	0.0	0.0	0.0	0.0	2.7[d]	1.3
Bipolar disorder	0.0	0.0	0.0	0.0	3.1[d]	1.4
Anxiety disorders	29.3	6.5	8.1[c]	3.5	18.6	2.9
Avoidant disorder	1.5	1.5	1.4	1.4	1.3	0.8
Overanxious disorder	16.2	5.1	1.8[c]	1.8	7.6	1.8
Separation anxiety	1.5	1.5	1.4	1.4	3.4	1.2
Panic disorder	11.0	5.3	0.0[d]	0.0	7.1	2.3
Agoraphobia	4.9	3.4	1.9	1.9	4.6	1.6
Phobic disorder (social/simple)	10.1	4.4	0.0[d]	0.0	7.6	2.0
Obsessive-compulsive disorder	0.0	0.0	0.0	0.0	0.7	0.7
Substance use disorders	17.8	6.2	13.4	5.7	27.6	3.7
Alcohol abuse	9.9	4.7	10.8	5.2	8.8	2.3
Alcohol dependence	2.8	2.8	2.5	2.5	14.2[c]	2.8
Drug abuse	0.0	0.0	0.0	0.0	0.0	0.0
Drug dependence	7.2	4.0	0.0	0.0	9.1	2.3
Somatization disorder (Briquet)	0.0	0.0	0.0	0.0	0.0	0.0
Enuresis	0.0	0.0	0.0	0.0	0.0	0.0
Anorexia nervosa	2.8	2.8	0.0	0.0	1.2	0.8
Autism or other pervasive developmental disorder	0.0	0.0	0.0	0.0	0.0	0.0
Psychotic disorders not elsewhere classified	0.0	0.0	0.0	0.0	0.7	0.7
Schizophrenia	2.7	2.6	0.0	0.0	2.7	2.1
Tics	1.5	1.5	1.4	1.4	0.8	0.6
Language disorders	3.2	2.2	1.4	1.4	0.4	0.4
Sleepwalking or sleep terror disorder	0.0	0.0	1.4	1.4	0.4	0.4
Tobacco dependence	32.8	7.3	17.8	5.7	38.2	3.8
Stuttering	6.3	3.0	7.2	3.1	3.0	1.1
School dysfunction	29.3	5.9	11.0[d]	4.3	20.8	2.9
Repeated grade	10.0	3.9	5.8	3.3	11.6	2.3
Special class	6.5	3.2	0.0[d]	0.0	1.0	0.7
Extra help	21.9	5.4	4.7[c]	2.7	9.6[d]	2.1

[a] Statistical differences refer to comparisons with the relatives of the girls with attention deficit disorder.
[b] As reported elsewhere (11).
[c] $p<0.01$.
[d] $p<0.05$.

families of the boys and girls with attention deficit disorder, significantly higher risks were found in the boys' families for alcohol dependence (z=2.9, p=0.004), dysthymia (z=2.0, p=0.04), and bipolar disorder (z=2.0, p=0.04). In addition, a smaller proportion of the boys' relatives had required extra help during their school years (z=2.1, p=0.03).

DISCUSSION

Our results indicate that the first-degree relatives of clinically referred girls with attention deficit disorder have a significantly higher risk for attention deficit disorder than the relatives of normal girls. The familial risk for attention deficit disorder in this study was similar to the risk reported in an identically ascertained and evaluated sample of boys with attention deficit disorder (11). As found for the boys, the higher risk for attention deficit disorder remained significant after statistically controlling for gender and generation of relative, intactness of family, and social class, indicating that irrespective of gender, the familial transmission of attention deficit disorder could not be attributed to the potentially confounding effects of these factors. However, it is notable that, compared to the parents of normal girls, the parents of the girls with attention deficit disorder were more likely to be separated or divorced. Thus, further work is needed to clarify the association between intactness of family and the familial transmission of attention deficit disorder.

In addition to the similar risks for attention deficit disorder among the families of the boys and girls with the diagnosis, the families were also strikingly alike in their risks for other psychiatric disorders. The families of both girls and boys with attention deficit disorder had higher than normal risks for antisocial, affective, and anxiety disorders. The only differences between the girls' and boys' families were the higher risk for alcohol dependence among the boys' relatives and the higher risk for school dysfunction among the girls' relatives. Although the difference was not statistically significant, the boys had a higher rate of comorbid conduct disorder than the girls. Since we previously reported that the risk for substance abuse among the relatives of the boys with attention deficit disorder was accounted for by the presence of comorbid conduct disorder in the proband boys (26), the higher risk for alcohol dependence in their families could be due to their higher rate of conduct disorder. The high risk for school dysfunction among relatives of girls with attention deficit disorder is consistent with the fact that school failure is a well-known and frequently reported complication of the disorder (27, 28). It is also consistent with reports that girls with attention deficit disorder are more likely to manifest cognitive impairments than boys with the disorder (7).

While the high risks for major depression and antisocial disorders among relatives of girls with attention deficit disorder confirm previously reported findings in boys (10–16), a high risk for anxiety disorders in the relatives of boys with attention deficit disorder has only been found recently (11). Although the relatives of both the boys and girls in our studies were at high risk for anxiety disorders, the risk was especially high for the girls' relatives. This is consistent with the higher rates of comorbid phobic disorders among the girls than among the boys. Further work is needed to disentangle the effects of gender on psychiatric comorbidity in probands with attention deficit disorder and their relatives.

Our findings should be interpreted with caution for several reasons. First, our findings from a clinically referred sample of patients with attention deficit disorder may not generalize to other children with the same disorder. Clinically referred patients with attention deficit disorder are more likely to be severely ill and to seek treatment from physicians or other health professionals than nonreferred ones. However, the rates of comorbidity found in this sample of clinically referred girls are similar to those observed in recent studies of nonreferred children, suggesting that our girls with attention deficit disorder may, in many respects, be representative of children with attention deficit disorder in the community (1, 2). Second, the retrospective diagnosis of attention deficit disorder in adults is more difficult to make than a diagnosis in childhood. Nevertheless, a recent report (29) indicated that it is possible to validly diagnose this disorder in adolescents and adults by using structured interview techniques. Third, the fact that all but one of the girls with attention deficit disorder in our study and 90% of the boys had hyperactivity may limit the generalizability of the results to children without hyperactivity. Unfortunately, our sample of probands with attention deficit disorder without hyperactivity was too small (one girl, seven boys) to support meaningful comparisons with the hyperactive probands. Fourth, we did not incorporate direct teacher reports into our diagnosis of attention deficit disorder. However, the probands with attention deficit disorder in this study had severe symptoms requiring clinical intervention. Their symptoms were manifested at home and in school, according to the interviews with the mothers.

Finally, our sample of normal girls was screened for the absence of psychiatric and medical disorders. Additional research using a comparison group matched on pertinent demographic variables and differing primarily in the diagnosis of attention deficit disorder would provide useful information.

In summary, our findings indicate that attention deficit disorder is highly familial in clinically referred girls with attention deficit disorder. In addition, their families are also at high risk for antisocial disorders, major depression, anxiety disorders, and school dysfunction. These familial risks are consistent with those found in the families of boys with attention deficit disorder. The similar pattern of psychiatric disorders in the families of girls and boys with attention deficit disorder suggests that, to a substantial degree, familial etiological factors in attention deficit disorder may not differentiate the two genders. Further understanding of familial differences may elucidate the reasons for gender differences in attention deficit disorder.

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Axis II Comorbidity in Substance Abusers

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Objective: *To assess the complex relationship between substance abuse and personality disorders, the authors determined the prevalence of personality disorders in a group of middle-class substance abusers and compared the subjects who had personality disorders with those who did not.* Method: *The subjects were drawn from patients consecutively admitted to an inpatient substance abuse program in a private psychiatric hospital; they were the first 100 who agreed to participate. Substance dependence was diagnosed according to* DSM-III-R, *and the patients were assessed with the Structured Clinical Interview for DSM-III-R Personality Disorders, Alcohol Use Inventory, MMPI, Health and Daily Living Form, Shipley Institute of Living Scale, and measures of chemical use and life satisfaction.* Results: *Of the 100 substance abusers, 57 had personality disorders. These patients differed significantly from the 43 patients without personality disorders in several ways: they had greater involvement with illegal drugs, had different patterns of alcohol use, had greater psychopathology, were less satisfied with their lives, and were more impulsive, isolated, and depressed.* Conclusions: *Because of the marked differences between the substance abusers with and without personality disorders, a uniform approach to substance abuse treatment may be inadequate.*

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In a study by Helzer and Pryzbech (1) psychiatric diagnoses were more prevalent among alcoholics than nonalcoholics. The only axis II disorder addressed was antisocial personality disorder. Unlike axis I disorders, which may respond to specific treatments, the personality disorders do not yield to symptom-specific interventions and are likely to complicate the treatment of a substance use disorder (2).

For years, typologies of alcoholics have been presented in the hope of improving treatment. Cloninger (3) divided alcoholics into those in whom onset occurs after age 25 and for whom environmental factors play a precipitating role (type 1) and those whose onset occurs before age 25, who have novelty-seeking traits, and for whom heredity is considered a major factor (type 2). Subsequent studies (4, 5) have failed to validate this type 1/type 2 dichotomy.

The objective of the present study was to explore the complex relationship between personality variables and substance use disorders. We determined the prevalence of personality disorders in a group of middle-class substance abusers and compared those who had personality disorders with those who did not.

METHOD

The subjects were 100 inpatients consecutively admitted to a substance abuse program in a private psychiatric hospital between September 1987 and December 1988. Excluded from the study were patients who were acutely psychotic, who were clinically impaired by organic brain damage, or who were less than 18 years old and eight patients who refused to participate.

Data were collected at least 2 weeks after admission to the hospital. After substance dependence had been diagnosed according to DSM-III-R criteria, the patients were assessed with the Structured Clinical Interview for DSM-III-R Personality Disorders (SCID-II) (6). Each author interviewed one-third of the subjects. The SCID-II is based on the DSM-III-R criteria for personality disorders. Throughout each interview an attempt was made to distinguish between behaviors and attitudes that characterized the patient generally and behaviors and attitudes that were consequences of intoxication. At the beginning of each interview, the interviewer said, "I'm going to ask you some questions about the kind of person you are, that is, how you have generally felt or behaved. I know there have been times when you've been involved with alcohol or drugs. I'm

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TABLE 1. Significant Differences in Substance Abuse and Psychological Ratings Between Substance Abusers With and Without Personality Disorders

	With Personality Disorders (N=57)		Without Personality Disorders (N=43)		Two-Tailed t Test With Bonferroni Correction		
Measure	Mean	SD	Mean	SD	t	df	p<
Alcohol Use Inventory							
Compulsive alcohol use	5.40	2.75	3.58	1.89	3.78	89	0.001
Use of alcohol to manage mood	5.29	2.77	4.25	2.02	2.08	89	0.04
Use of alcohol to enhance functioning	4.58	2.75	3.45	2.25	2.10	90	0.04
Pervasiveness of alcohol in one's life	3.11	1.84	2.22	0.66	3.22	67	0.002
Lifetime substance abuse							
Marijuana	4.19	2.84	2.93	1.89	2.64	95.5	0.01
Amphetamines	2.79	2.35	1.76	1.56	2.61	95.5	0.01
Cocaine	3.72	2.48	2.41	1.97	2.79	96	0.01
LSD	2.35	1.56	1.59	0.89	3.06	92	0.01
Opiates	1.56	0.88	1.19	0.64	2.37	96	0.05
MMPI							
Depression	70.63	16.27	64.33	12.99	2.08	97	0.05
Psychopathic deviate	77.48	11.35	70.19	10.19	3.31	97	0.001
Paranoia	67.79	11.21	61.19	8.30	3.37	97	0.001
Psychasthenia	69.23	13.05	60.33	11.10	3.59	97	0.001
Schizophrenia	71.93	14.77	58.28	9.73	5.53	95	0.001
Mania	65.77	13.28	59.63	9.82	2.64	97	0.01
Introversion	56.77	13.17	47.93	6.64	4.35	85.3	0.001
Health and Daily Living Form							
Global depression	43.05	16.50	28.40	13.52	4.70	97	0.001
Negative life changes	3.00	2.50	1.70	1.80	2.92	95	0.01
Avoidance as a means of coping	11.51	4.06	8.33	3.96	3.89	97	0.001
Emotional discharge as a means of coping	8.16	3.45	6.36	3.37	2.59	97	0.01
Problem solving as a means of coping	6.21	3.93	7.86	3.36	2.19	97	0.05
Satisfaction questionnaire							
Overall life	3.60	1.25	2.93	1.02	2.83	97	0.05
Social life	3.40	1.24	2.81	0.86	2.81	97	0.01
Emotional health	3.70	0.99	3.21	0.90	2.50	97	0.01
Relationships	3.11	0.99	2.38	1.03	3.52	97	0.001
Job and school performance	3.31	1.20	2.53	1.05	2.82	64	0.01

not talking about those times, and you should try to think about how you usually are when you are not involved with those substances." Using the SCID-II, all three authors blindly assessed the presence of personality disorder in 10 patients to determine interrater agreement. We obtained a Cohen's kappa of 0.90 (t=5.6, df=43). The probability of obtaining this result by chance is less than 0.001.

The patients completed the Alcohol Use Inventory (7), Minnesota Multiphasic Personality Inventory (MMPI), Health and Daily Living Form (8), Shipley Institute of Living Scale (9), a chemical use inventory, and a satisfaction questionnaire.

The Alcohol Use Inventory measures the perceived benefits, styles, and consequences of alcohol use. The Health and Daily Living Form measures health and social functioning. The Shipley Institute of Living Scale estimates intellectual functioning. The chemical use inventory measures lifetime frequency of use of 38 chemicals on an 8-point rating scale. The satisfaction questionnaire rates nine life areas. A chi-square analysis was done on the demographic data when deemed appropriate. We used t tests with the Bonferroni correction to test differences between the personality disorder group and the group without personality disorders on selected variables. A criterion probability of 0.05 was selected to assign significance to the difference between groups.

RESULTS

According to the SCID-II, 57% of the 100 consecutively admitted patients each had at least one personality disorder, and 43% did not meet the criteria for personality disorders.

There were no significant differences in gender or race between the groups with and without personality disorders. The personality disorder group was significantly younger (mean±SD=31±10 years) than the group without personality disorders (38±13 years). The subjects with personality disorders had significantly less education (mean±SD=13.6±2.3 years) than the group without personality disorders (15.2±3.6 years). The personality disorder group was less likely to be married (68%, N=39) than the group without personality disorders (51%, N=22) (χ^2=6.2, df=2, $p<0.05$).

The specific personality disorders of the 57 patients with personality disorder were as follows: cluster A—paranoid (N=7); cluster B—antisocial (N=3), borderline (N=17), histrionic (N=6), narcissistic (N=4); cluster C—avoidant (N=2), dependent (N=4), obsessive-compulsive (N=2), passive-aggressive (N=5). In addition, five had self-defeating personality disorder, and two had personality disorders not otherwise specified. Axis I diagnoses other than substance use disorder were found in 44% of the personality disorder group (N=25) and 49% of the group without personality disorders (N=21) (a nonsignificant difference). The axis I diagnoses in both groups were primarily affective disorders.

The subjects with personality disorders were more extensively involved in substance abuse than the subjects without personality disorders (see table 1). On the Alcohol Use Inventory the personality disorder group scored significantly higher on the measures of compulsive alcohol use, use of alcohol to manage mood, use of alcohol to enhance functioning, and pervasiveness of alcohol in one's life. On the chemical use inventory the personality disorder group showed significantly greater lifetime use of marijuana, amphetamines, cocaine, LSD, and opiates.

There was no significant difference in IQ, estimated according to the Shipley Institute of Living Scale, between the group with personality disorders (mean± SD=118±18) and the group without personality disorders (121±16). As shown in table 1, the personality disorder group had standardized scores on the MMPI that were significantly higher on all of the clinical subscales except 1, 3, and 5 (hypochondriasis, hysteria, and masculinity/femininity). On the Health and Daily Living Form the personality disorder group scored significantly higher on global depression, negative life changes, avoidance as a means of coping, and emotional discharge as a means of coping. The group without personality disorders scored significantly higher on problem solving. On the satisfaction questionnaire the personality disorder group indicated that they were significantly less satisfied with the overall quality of their lives, social lives, emotional health, relationships, and job and school performance.

DISCUSSION

This study documents the clinical heterogeneity of a group of substance abusers. Of 100 consecutively admitted patients, 57 each had at least one personality disorder. The group with personality disorders had greater involvement with illegal drugs and differed significantly in patterns of alcohol use. Further, those in the personality disorder group had greater psychopathology, were less satisfied with most areas of their lives, and were more impulsive, isolated, and depressed than those in the group without personality disorders.

A uniform approach to treatment of substance-abusing patients may be inadequate even with socioeconomically homogeneous subjects. Because of the marked differences in dysfunction within our substance-abusing group, it seems important to individualize treatment for these patients.

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Efficacy of Behavioral Versus Triazolam Treatment in Persistent Sleep-Onset Insomnia

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Objective: This study compared differential effects of behavioral therapy and triazolam in a clinical population with sleep-onset insomnia. Triazolam was hypothesized to decrease sleep latency and frequency and duration of awakenings, with some effects during the first night's administration. But at follow-up, sleep measures were predicted to return to baseline levels. Behavioral treatment was hypothesized to effect sleep after 2 or more weeks of training which persisted at follow-up. Method: Thirty patients with average sleep latencies of 81.48 minutes, who reported chronic insomnia for an average of 2.6 years, were randomly assigned to one of two treatment groups: behavioral stimulus control/relaxation training and triazolam. Results: Both treatments decreased sleep latency but differentially. Triazolam was effective immediately but maintained only some gains at follow-up. Behavioral treatment decreased sleep latency beginning the second week, when subjects expected no improvement, with gains maintained at follow-up. Comparisons showed that triazolam group latencies returned toward baseline, while behavioral group gains were maintained at follow-up. Conclusions: Triazolam treatment showed superior immediate treatment effects, while behavioral treatment showed superior treatment effects at follow-up, effects that accrued during the training period and differentially persisted at follow-up. One treatment strategy implied by these results would be to combine these two interventions concurrently. This would seem to use the immediate effects produced by the medication until the behavioral skills were learned, at which point medication would be terminated. This strategy could offer immediate relief and sustained effects at drug termination.

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Persistent psychophysiological disorders of initiating and maintaining sleep are experienced by millions (1) and are defined as sleep difficulties of more than 3 weeks that are not attributed to medical or psychiatric causes (2). For such sleep-onset insomnia, two types of treatment have been effective: drug therapy with hypnotic sedatives (3, 4) and behavior therapy (5–7). Habituation, psychological dependency, addiction, and iatrogenic sleep disturbance have been reported with continued use of hypnotics (8), and most hypnotics become ineffective after short-term use (1–2 weeks) (8, 9). Flurazepam has been prescribed for insomnia when extended efficacy was necessary (6) and has become a standard for other hypnotic agents. However, its mean half-life of 65.2 hours and cumulative plasma buildup have been a concern (10). An alternative to flurazepam is triazolam, with a mean half-life of 2.2 hours (3), which eliminates cumulative plasma levels in sequential dosing. Compared to flurazepam in studies of 1–84 days, triazolam was equally or more effective in reducing sleep latencies (11–14). However, hypnotics appear best suited for relatively short-term use (9). With insomnia of several years' duration, alternative treatment may be more appropriate.

Behavior therapies are effective for sleep-onset insomnia (6, 7, 15). Relaxation training has been effective in college subjects with mild sleep disturbance (16, 17), and an ingenious counterdemand control procedure has been devised to measure and control these effects while monitoring results at follow-up (17). Relaxation training efficacy, using counterdemand control and follow-up, was replicated (5). These controls have become standard in subsequent studies. Other studies found that relaxation training was effective with more severe insomnia (18–21), and an analysis of

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The Upjohn Company provided the triazolam used in this study.

its necessary components demonstrated that muscle tension and release were unrelated to outcome (22).

A second behavioral procedure called stimulus control has also been effective regardless of severity of insomnia (23). A variant of the stimulus control procedure is the technique of sleep restriction therapy, in which the focus is on maximizing the quality of sleep by consolidating sleep into a limited block of time (24). Studies have compared behavioral treatments and combinations of treatments (25–27). Shealy (28) examined behavioral treatment of mild and moderate insomnia (latencies of 32 and 64 minutes, respectively). Seventy college women were assigned to one of five treatment and control groups. Results showed that stimulus control plus relaxation and relaxation alone were effective. However, the first group showed more effectiveness in a shorter period of time.

The purpose of the present study was to compare the effectiveness of relaxation plus stimulus control (28) with triazolam for sleep-onset insomnia in a clinical population. The intent was less to demonstrate efficacy of each treatment than to compare their differential effects. It was hypothesized that triazolam would decrease sleep-onset latency and the frequency and duration of awakenings. We hypothesized effects on sleep measures after the first night's administration. But we predicted that at follow-up, sleep measures would return to baseline.

From previous research (28) showing that relaxation would not significantly reduce awakening frequency or duration, we hypothesized that only sleep latency would decrease. Since both behavioral interventions require time to become effective, we hypothesized that their efficacy would be manifested during the second and third weeks of training. However, we hypothesized that once learned, these techniques would maintain gains at follow-up.

METHOD

Subjects

The subjects were selected from 73 respondents to newspaper advertisements. The 13 men and 17 women were 22–43 years of age (mean=32 years). The mean sleep-onset latency of 81.48 minutes averaged 2.6 years' duration. Applicants were excluded for the following conditions: receiving other insomnia treatment; current use of hypnotics, antihistamines, or psychotropic medication; substance abuse; major affective disorder, psychoses, organic brain syndrome, or mental retardation, according to *DSM-III* criteria; history of allergic reactions to benzodiazepines; medical problems contraindicating triazolam use, such as liver disease and impaired renal functioning; chronic pain; pregnancy, breast-feeding, or sexual activity by women not using contraceptives; and nonpsychophysiological disorders of initiating and maintaining sleep such as restless leg syndrome, nocturnal myoclonus, and sleep apnea.

Applicants between the ages of 19 and 45 were accepted for the study if their sleep latencies had exceeded 60 minutes at least 3 days a week for 6 months. Thirty subjects met these criteria, which were assessed by self-report, psychological testing, and interview. Forty-three applicants were rejected, 12 because of psychiatric disorders. All 30 subjects who were selected completed the study.

Procedure

The Screening Check List screened for inclusion and exclusion criteria. The Sleep Behavior Questionnaire (28) combined items in other questionnaires (29, 30) that were found to correlate well with electrophysiological sleep measures. The Haynes et al. questionnaire (30) had a test-retest reliability of 0.86. The Daily Sleep Questionnaire obtained information concerning the previous night's activities and sleep, and the Daily Sleep and Relaxation Practice Questionnaire was exactly the same as the Daily Sleep Questionnaire except for two added questions concerning subjects' relaxation practice (28). The Stanford Sleepiness Scale, used during baseline, is an 8-point rating scale for sleepiness that ranges from 1—"Alert, wide awake, energetic" to 7—"Cannot stay awake. Sleep onset soon" and 8—"Asleep." It divides each day into 12 2-hour epochs for rating purposes.

Subjects experienced the following sequence: telephone screening, initial assessment, baseline sleep data collection, treatment, and 1-month follow-up. Procedures common to both treatment groups were telephone screening, initial assessment, and baseline sleep data collection. In telephone screening, subjects responded to newspaper advertisements by calling the investigator. The Screening Check List imposed screening criteria, and 23 subjects were excluded. In the initial assessment subjects completed the Sleep Behavior Questionnaire, MMPI, and Beck Depression Inventory and received a psychiatric interview. Because subject selection took several months, the MMPI, Sleep Behavior Questionnaire, and Beck Depression Inventory were repeated for subjects who were evaluated more than 1 month before data collection. Informed consent forms were given, and a brief description of each treatment was provided. During baseline sleep data collection subjects completed daily, for 2 weeks, the Daily Sleep Questionnaire upon awakening and the Stanford Sleepiness Scale. Seven subjects were excluded on the basis of baseline measures of daily sleep latency. Subjects were then stratified by sleep latency data obtained from the Daily Sleep Questionnaire during baseline and randomly assigned to triazolam and behavioral groups (15 per group). When possible, spouse and roommate ratings of the subjects' sleep latency were obtained on the Sleep Behavior Questionnaire, 2 nights a week throughout all phases, as a reliability check for self-report measures. Complete spouse-roommate data were obtained on three subjects in the behavioral group and four subjects in the triazolam group.

Treatment consisted of six sessions, two per week for 3 weeks, with subjects seen in three five-member groups for each treatment; the sessions were conducted in a comfortably appointed group room. Two investigators (H.Y.M. and P.K.S.) were present during all sessions. After consent forms were signed, the pretreatment assessment of therapist effectiveness and treatment credibility was completed (27). Other procedures were different for each treatment.

Behavioral treatment groups met in a dimly lit room and were seated in chairs or sofas. Counterdemand and positive demand instructions were given. Thus, subjects were told that improvement was not expected for 2 weeks but would begin during week 3. Passive relaxation instructions (nonmuscle flexion and release) used by Haynes et al. (30) and Shealy (28) were presented on a stereo system. After the relaxation procedure, subjects were instructed to practice relaxation twice a day for 15 minutes, once just before sleep. The second session taught the stimulus control procedure, including principles and specific instructions (26). Subjects were given five steps to follow.

1. Go to bed when you are tired, go to bed about the same time each evening, and arise at about the same time each morning.
2. If you do not fall asleep within 30–45 minutes after lying down, get up, go to another room, and do something until you get sleepy; then return to bed. Repeat continuously if you do not fall asleep within 30–45 minutes.
3. Do not do anything in bed except sleep and have sexual relations. Do not watch television, read, eat, etc. in bed.
4. Do not eat or drink fluids after 7:00 p.m., especially beverages containing caffeine.
5. Take no naps.

The remaining four sessions were divided into 15–20-minute periods; the first addressed problems with stimulus control procedures, and the second was for relaxation training. Each subject completed the Daily Sleep and Relaxation Practice Questionnaire each morning during treatment and at follow-up. At the last session subjects were given follow-up sleep questionnaires and a credibility rating to be completed the fifth week after treatment and returned by mail.

Triazolam groups met in the brightly illuminated behavioral group room. In session 1 subjects were presented with the rationale for and mechanisms of drug treatment, and side effects and precautions were discussed. Leaders answered questions about medication and gave instructions for the medication regimen. Subjects were instructed to take 0.5 mg of triazolam nightly, 30 minutes before bedtime. They were given seven single-unit doses of triazolam with written instructions in a sample packet. In five subsequent 30–40-minute sessions, medication was dispensed and sleep and drug mechanisms related to sleep were discussed. Possible side effects were reported, and investigators monitored signs of untoward reactions. At the end of treatment, triazolam was withdrawn following a slow tapering regimen (31). Doses were reduced to 0.25 mg for 3 nights and 0.125 mg for 4 nights and were then discontinued. Subjects completed the Daily Sleep Questionnaire each morning during treatment. Follow-up credibility rating forms and Daily Sleep Questionnaires were given to subjects in the last session for completion and mailing 5 weeks later.

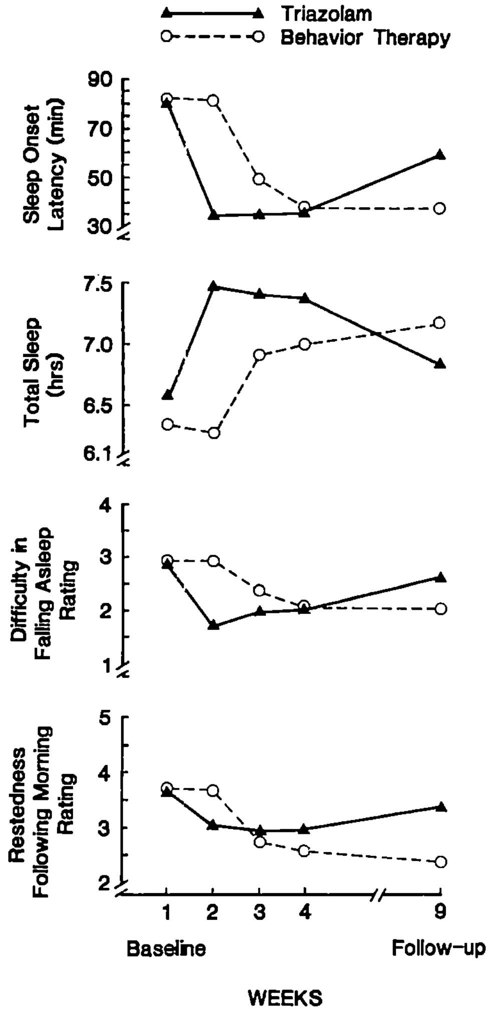
RESULTS

Average weekly sleep indices were calculated from ratings on the Daily Sleep and Relaxation Practice Questionnaire and the Daily Sleep Questionnaire for the behavioral and triazolam groups, respectively. Indices included sleep-onset latency (minutes), number of awakenings, duration of awakenings (minutes), total sleep (hours), difficulty falling asleep (rated on a 4-point scale), and restedness the following morning (rated on a 5-point scale; lower scores represent improvement). Weekly means for the most sensitive indices are presented in figure 1. Mixed-model analyses of variance were employed in analyzing the differential effects of the two treatments on the dependent variables. Treatment condition served as the between-groups factor, with weeks being the repeated, within-subjects factor.

The Treatment by Weeks interaction effect was significant for four of the six dependent variables. Number of awakenings and time awake were not influenced by the treatment and showed no significant changes over time. Significant changes over the course of the study in sleep-onset latency, restedness the following morning, total sleep, and difficulty falling asleep were also supported by a main effect for the Weeks factor. Main effects due to treatment failed to emerge for any of the dependent variables. Follow-up simple effects analyses were conducted to further analyze the Treatment by Weeks interactions for sleep-onset latency, restedness the following morning, total sleep, and difficulty falling asleep.

A significant Week by Treatment interaction ($F=20.30$, $df=4, 112$, $p<0.0001$) and main effect for Weeks ($F=39.56$, $df=4, 112$, $p<0.0001$) emerged for sleep-onset latency. At week 1, sleep-onset latency was similar for both treatment groups. By week 2 subjects in the triazolam group demonstrated significantly shorter sleep-onset latency than did those in the behavioral group, so that latencies were similar for both treatment groups at week 4. By follow-up 5 weeks later, sleep-onset latency had become longer in the triazolam group than in the behavioral treatment group ($F=8.45$, $df=1, 28$, $p<0.01$). Thus, in general, both treatments resulted in improved sleep-onset latency over the course of the study; but by follow-up sleep-onset latency had lengthened in the triazolam group, while the behavioral group sustained reductions in sleep-onset latency (see figure 1).

FIGURE 1. Mean Weekly Values on Sleep Measures for Subjects With Sleep-Onset Insomnia Who Were Given Triazolam (N=15) or Behavior Therapy (N=15)



Ratings of restedness the following morning demonstrated significant changes over the course of the study ($F=26.53$, df=4, 112, $p<0.0001$). Week 1 ratings were the same across treatments. At week 2 the triazolam group showed improvements that represented better (lower) restedness ratings than those among the behavioral group ($F=3.97$, df=1, 28, $p<0.05$). Ratings improved after week 2 for both groups and were similar until week 4, when the behavioral group demonstrated significantly greater restedness than did the triazolam group ($F=13.76$, df=1, 28, $p<0.01$), whose ratings had returned to levels similar to those observed at baseline.

Number of hours of sleep showed significant changes over the course of the study ($F=20.82$, df=4, 112, $p<0.0001$) and differed for the two treatment groups ($F=16.82$, df=4, 112, $p<0.0001$). The triazolam group's sleep time improved the most from week 1 to week 2, and their total sleep at both week 2 ($F=26.49$, df=1, 28, $p<0.0001$) and week 3 ($F=4.71$, df=1, 28, $p<0.05$) was significantly greater than that of the behavioral group. The behavioral group, on the other hand, evidenced a linear improvement in total sleep time from baseline to follow-up, and at follow-up its total sleep time was greater than that of the triazolam group, although the difference was not statistically significant. Both groups evidenced significant improvements from baseline to follow-up (triazolam: $F=5.48$, df=1, 14, $p<0.05$; relaxation: $F=31.88$, df=1, 14, $p<0.0001$). The behavioral group demonstrated a mean±SD increase from 6.33 ± 0.71 to 7.15 ± 0.74 hours, and the triazolam group had a slight increase from 6.57 ± 0.62 to 6.84 ± 0.80 hours of sleep over the course of the study.

Treatment condition and duration of treatment interacted to influence ratings of difficulty falling asleep ($F=41.32$, df=4, 112, $p<0.0001$). The triazolam group showed the greater decrease in difficulty falling asleep from baseline to week 2 (drop of 1.22 points). The group's ratings then increased slowly from week 2 through follow-up until they had almost returned to baseline level of difficulty ($F=1.88$, df=1, 14, $p>0.05$). The behavioral group's ratings showed a steady decrease from week 2 through follow-up, which represented a significant improvement over baseline ($F=74.30$, df=1, 14, $p<0.0001$). The between-group differences measured at follow-up indicated a significant advantage due to behavioral training ($F=12.83$, df=1, 28, $p<0.001$).

Seven subjects (four in the triazolam group and three in the behavioral group) were asked to have their spouses or roommates complete ratings of the amount of difficulty the subjects experienced in falling asleep during the course of the study. This allowed us to compare an observer's rating on this variable with subjects' subjective ratings of difficulty falling asleep. Correlations for subject and spouse-roommate ratings were 0.94 ($p<0.01$) for the triazolam group and 0.96 ($p<0.01$) for the behavioral group.

DISCUSSION

The most important results showed differential effectiveness and superiority of behavioral treatment over triazolam for insomnia at follow-up. This finding was anticipated and is consistent with our hypotheses. It is compatible with a literature of studies that lack follow-up of 1-month's duration (3).

While behavioral treatment showed no effects during week 1, it significantly reduced sleep latencies during the counterdemand period. Its 45% latency reduction in week 2 where there was a counterdemand demonstrated its power when expectations were induced to negate positive gains in sleep indices.

One possible explanation for the efficacy of both treatments needs to be considered. Was it possible that actual sleep patterns did not change, and self-report measures reflected a change in perception of improved sleep? No electrophysiological sleep measures were employed, so this possibility needs to be addressed. Spouse-roommate ratings, highly correlated with subject indices, are inconsistent with this notion. Occurrence of other potentially confounding variables—frequency and duration of awakening—was so low that their confounding impact was negligible. But because of the paucity of awakenings, generalization to a population with sleep-onset insomnia with frequent awakenings may be inappropriate.

Because treatments were viewed with maximal credibility and expectations for success, and both therapists were seen as very competent and warm, between-group differences cannot be attributed to these variables. Within-group change probably was affected by the subjects' positive view of the therapists and high expectations for change. Thus, change in sleep measures was likely a function of a treatment situation that maximized opportunity for change.

This study employed two research-based effective interventions for sleep-onset insomnia and was designed to *compare* rather than establish their efficacy. However, since parallel placebo control groups were not employed, it is possible that the efficacy of either treatment was based primarily on nonspecific placebo effects. Mitler et al. (32) have demonstrated that many chronic insomniacs improve with placebo treatment during the course of a parallel comparison with an active drug. Arguing against such placebo effects is the use of the counterdemand control in the behavioral group. Such specific predicted results with subjects induced to believe the opposite effects is a compelling argument against placebo effects for that group. Yet it is true that a more complete experimental design to directly address questions of treatment efficacy in the future should employ parallel placebo control groups.

To our knowledge this is the first published study comparing behavioral therapy with hypnotic/sedative treatment for insomnia. Our results indicate that behavioral treatment is a viable alternative for persistent, psychophysiological, sleep-onset insomnia and may be preferable, considering its sustained effectiveness. Our results are consistent with increasing awareness of behavioral variables in insomnia regulation and the need to change behavioral variables if intervention is to have lasting efficacy (7, 33, 34). Behavioral treatment is clearly preferable with individuals who are sensitive or allergic to sleep medication, prone to drug abuse, taking medications that contraindicate use of sedative hypnotics, prefer no medication, are pregnant or breast-feeding, and who have insomnia of long-term duration.

The role of hypnotics in the treatment of chronic insomnia is uncertain, but careful use could benefit patients as part of a well-defined clinical strategy. One strategy is to administer medications concurrently with behavioral therapy until behavioral skills are learned, at which point medication is terminated. This strategy, recommended by Morin and Kwentus (7), could offer immediate relief and sustained effects at drug termination. This would be a fruitful area for further research.

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Controlled Comparison of Buspirone and Clomipramine in Obsessive-Compulsive Disorder

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Eighteen outpatients with obsessive-compulsive disorder were treated with either buspirone, a partial serotonin agonist, or clomipramine, a serotonin uptake inhibitor, in a double-blind, random-assignment study. Both drugs led to statistically significant and similar improvements in scores on the Yale-Brown Obsessive-Compulsive Rating Scale and other obsessive-compulsive and depression scales. This preliminary result warrants further exploration with a larger sample and other serotonergic agents.

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The efficacy of clomipramine in the treatment of obsessive-compulsive disorder has been clearly established (1). The superiority of clomipramine to placebo and to other tricyclics that have equivalent antidepressant efficacy has been hypothesized to be related to clomipramine's inhibition of serotonin uptake. This hypothesis is supported by the efficacy in obsessive-compulsive disorder of more highly selective serotonin reuptake inhibitors, such as fluoxetine and fluvoxamine (1).

In this study we evaluated the therapeutic efficacy of buspirone, another agent with prominent serotonergic properties that has demonstrated anxiolytic and putative antidepressant effects (2). Anxiety and depressive symptoms often coexist with obsessive-compulsive symptoms and, although benzodiazepines seem to be of minimal therapeutic value in obsessive-compulsive disorder, no controlled trials with buspirone or related azapirones have been reported to our knowledge.

METHOD

Twenty outpatients who met the *DSM-III-R* criteria for obsessive-compulsive disorder participated in this random-assignment, double-blind crossover study. Eighteen of the 20 patients completed the study; one patient dropped out because of side effects during clomipramine treatment, and the other dropped out because of clinical deterioration during buspirone treatment. The patients were in good general health, had normal physical examination findings and laboratory test results, and had no noteworthy medical history abnormalities. Written consent for participation was obtained.

On admission each of the patients had experienced obsessive-compulsive symptoms for a minimum of 1 year. The mean±SD age of the group was 35±9 years, and the mean age at symptom onset was 18±8 years. A minimum rating of 4 on the NIMH global obsessive-compulsive scale was required for inclusion of the patient in the study.

Clomipramine, buspirone, and placebo were placed in identical capsules. The patients were free of psychotropic drugs for a minimum of 2 weeks before the initial open baseline rating, and they were rated again after taking placebo for 2 weeks. Over the next 2 weeks administration of the active drugs began, and each patient's dose was increased to the maximum that could be tolerated, up to 250 mg/day for clomipramine

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TABLE 1. Rating Scale Scores of Obsessive-Compulsive Patients Before and After a 6-Week Trial of Clomipramine (N=9) or Buspirone (N=9)

Scale and Group	Score				t[a]	Patients Who Had 20% Improvement in Score	
	Baseline		End				
	Mean	SD	Mean	SD	(df=17)	N	%
Yale-Brown Obsessive-Compulsive Rating Scale					5.21		
Clomipramine	24.44	4.51	17.67	4.97		6	67
Buspirone	22.89	4.79	16.78	6.46		5	56
NIMH obsessive-compulsive rating scale					6.51		
Clomipramine	29.61	4.54	21.22	5.49		5	56
Buspirone	29.89	6.66	19.22	5.97		7	78
Hamilton depression scale					3.18		
Clomipramine	13.28	4.70	9.33	4.58		6	67
Buspirone	13.22	5.83	9.89	6.75		5	56
NIMH global obsessive-compulsive rating scale					5.07		
Clomipramine	7.00	0.50	5.22	1.20		6	67
Buspirone	6.39	0.89	5.11	1.27		5	56
Yale-Brown severity measure					5.74		
Clomipramine	3.67	0.50	2.78	0.67		6	67
Buspirone	3.44	0.46	2.78	0.67		5	56

[a] Bonferroni-corrected. Significant difference ($p<0.05$) between baseline and final scores for each comparison.

and 60 mg/day for buspirone, during weeks 3–4 of the 18-week study. The mean±SD doses were 225±49 mg/day for clomipramine and 58±7 mg/day for buspirone. The patients achieved the maximum doses by day 14 and were maintained on these doses for the remaining 4 weeks of the 6-week phase 1 of the trial. This was followed by 4 days at half the maximum dose, 3½ weeks of placebo administration, and 6 weeks of the other drug (phase 2). Ratings were done at 2-week intervals. The interrater reliability between the two raters on all scales was high (interclass correlation coefficient=0.98, $p<0.001$). During the buspirone phase, one patient received lorazepam, 1–2 mg/day, for several days during weeks 3–4 for agitation and insomnia.

The rating scales used were the Yale-Brown Obsessive-Compulsive Rating Scale (range, 0–40) (3), the NIMH obsessive-compulsive rating scale (range, 0–56), the 24-item Hamilton Rating Scale for Depression, the NIMH global obsessive-compulsive rating scale (range, 0–15), and the Yale-Brown severity measure (range, 0–6), which is a global measure of severity taken from the Yale-Brown Obsessive-Compulsive Rating Scale.

Clinical improvement was defined as the percent improvement from baseline on each of the measures during phase 1. The criterion for a subject to be considered "improved" was a minimum of 20% improvement (4).

RESULTS

This study was intended to have a two-period, crossover design, and the data were to be analyzed by means of analysis of variance (ANOVA) with repeated measures in each period. The data were first analyzed to determine if carry-over effects from the end of phase 1 to the beginning of phase 2 were present (5). Carry-over effects were found; i.e., the subjects did not return to their baselines by the beginning of phase 2. Because of these carry-over effects, we followed Fleiss's recommendations (5) and analyzed only the phase 1 data. A parallel repeated measures statistical design was used to compare the efficacy of the two drugs during phase 1.

A repeated measures ANOVA revealed significant improvement in ratings of obsessive-compulsive disorder and depression over the 6 weeks of treatment for both drugs. For simplicity, only the ratings at baseline and at the end of phase 1 are presented in table 1. Bonferroni-corrected t tests showed a significant difference on each scale between baseline and the end of phase 1 for both drugs but no significant difference between drugs.

The magnitude of the response to drug during phase 1 was not correlated with age, sex, duration of obsessive-compulsive disorder, age at onset, previous benzodiazepine exposure, dose of clomipramine or buspirone, or mean serum level of clomipramine (201±117 ng/ml) or desmethylclomipramine (513±320 ng/ml). Most patients experienced minor side effects typical of both drugs, which were tolerated without much difficulty. Over one-half of the patients were judged "improved" (see table 1).

DISCUSSION

Buspirone and clomipramine were equally effective in the acute treatment of obsessive-compulsive disorder in the phase 1, 6-week parallel-design, double-blind trial. Both treatments were also associated with similar reductions in depression ratings. Phase 2, which represented the crossover portion of the design, was not analyzed because carry-over effects made it impossible to separate the roles of drug, week, and order in the analysis.

We are intrigued by the lack of consistent deterioration in both treatment groups during the placebo period between the two drugs (i.e., the carry-over effect). In similar studies of patients with obsessive-compulsive disorder, a 4-week clomipramine-free interval led to a substantial return of symptoms (6). In addition, Leonard et al. (7) reported that there was significant and distinct deterioration in 64% of their patients by 5 weeks, even though there was no distinct drug-free interval between the clomipramine and desipramine treatments.

Our results indicate a need for further study of buspirone in obsessive-compulsive disorder, and also reflect some of the pitfalls of a crossover design. To our knowledge, this is the first description of a controlled trial of buspirone in the treatment of obsessive-compulsive disorder. In a previous open trial (8), buspirone was ineffective in obsessive-compulsive disorder. However, in a recent open trial of buspirone augmentation of fluoxetine, the antiobsessional effects of combined treatment were superior to those of fluoxetine alone (9). It would also be valuable to explore whether buspirone's efficacy persists with longer treatment duration or lower doses. A recent report (10) suggested that patients may do equally well at lower doses of clomipramine after initial acute treatment.

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Book Forum

Nancy C. Andreasen, M.D., Ph.D., Editor

NEUROSCIENCE, NEUROPSYCHIATRY, AND NEUROLOGY

The Prefrontal Cortex: Anatomy, Physiology, and Neuropsychology of the Frontal Lobe, 2nd ed., *by Joaquin M. Fuster. New York, Raven Press, 1989, 320 pp., $85.00.*

Fuster's classic book on the prefrontal cortex first appeared in 1980. That book rapidly established itself as the landmark monograph on the prefrontal cortex and provided a major resource to clinicians, neuroscientists, and neurobiologists who were seeking a summary of our current knowledge about this important brain region. Neuroscience is a fast-moving field, however, and a new edition of *The Prefrontal Cortex* was soon needed. We now have it in a second edition of this major work.

The new edition has been updated in all respects. While it maintains the structure and emphasis of the earlier book, in that it is based on a strong foundation in anatomy and stresses the importance of the prefrontal cortex for temporal integration, a large amount of new material has been added. There is now a major section on neurotransmitters in which detailed information about the chemical anatomy of the prefrontal cortex is added to the chapter describing prefrontal circuitry. Once the chemical and connective structure has been outlined in the initial chapters, experimental studies are summarized. The effects of lesions on executive functions, emotions, motility, and perception are described, with a strong emphasis on the different effects that may be produced when lesions occur at an early age as opposed to later in life.

Lesion studies were among the earliest work used to explore the function of the prefrontal cortex, and this work has been extensively supplemented through techniques of neurophysiology, the domain for which Fuster himself is best known. Electrophysiology has been used to trace connections as well as to explore the role of the prefrontal cortex in learning, planning, memory, and the integration of information in relation to time. Much of the work using electrophysiology has involved primates.

An extensive chapter on human studies is also provided, however, which delineates the major "prefrontal syndromes" in human beings. In this chapter Fuster summarizes the effects of prefrontal abnormalities on affect and emotion (the apathetic syndrome versus the euphoric syndrome) as well as on attention, motility, and temporal integration. He also summarizes recent work done with neuroimaging, which has evaluated baseline blood flow and metabolism in the prefrontal cortex, measured the effects of cognitive challenges in normal individuals, and examined the "hypofrontality hypothesis" in major mental illnesses, particularly schizophrenia.

In his final chapter, Fuster presents his theory of the general function of the prefrontal cortex. For Fuster, the major function of the prefrontal cortex is the temporal organization of behavior. It serves as a major association region that supports a variety of cognitive functions as well as the three which are specific to the prefrontal cortex (provisional memory, preparatory set, and interference control).

An interesting figure in the second chapter of this book (covering the anatomy of the prefrontal cortex) highlights the importance of this brain region in human beings. In this figure the size of the prefrontal cortex is compared in cats, dogs, monkeys, and man, clearly showing that only human beings have a large and highly developed prefrontal cortex. This brain region is obviously the source of much of what makes us human. Understanding its structure and function permits us as psychiatrists to understand our patients and ourselves as human beings. Fuster's book is a major resource toward that end.

N.C.A.

Time and the Nervous System, *by William Gooddy. New York, Praeger, 1988, 192 pp., $37.95.*

Dr. Gooddy defines the purpose of the series of essays included in this book as "to suggest an outline for a new model of the world in which we find ourselves, based upon the concept of human self-awareness in time." He confronts us with large questions: What is time? How do we have a sense of time? What are the differences between personal time and government time? and How can we construct a philosophy of time that incorporates what we know of the role of the brain in mediating time sense? Despite their importance to an understanding of human existence, these questions are rarely raised in contemporary scientific literature.

This small provocative volume consists of 10 chapters, each discussing some aspect of human time and relating time to the function of the nervous system. Chapters address definitions of time, chronometric principles, clock-like activity in the nervous system, personal time, age and time, disorders of personal time, space-time disorientation, neurology and relativity, and a neurological cosmology. The recent chronobiological studies of seasonal mood disorders and circadian rhythms are barely mentioned; Dr. Gooddy is interested in the more abstract and encompassing biological principles that determine these surface phenomena.

The principal theme developed by Dr. Gooddy concerns the primacy of the human CNS as the origin of all our concepts of time, cosmology, and epistemology. He champions the uncontestable but often overlooked fact that all the deductions, explanations, and exemplifications of the sciences are neurologically derived from the system that mediates our existence and world experience. This emphasis on the primacy of brain function, however, does not lead him to a simple determinism. Dr. Gooddy attacks conventional determinism on statistical grounds, insisting that with 10 billion neurons, each connected directly to 2,000 others and each constantly changing, the notion of machine-like statistics with predictable results is untenable.

Dr. Gooddy also challenges the idea of absolute time ("the framework for an eternal universe in which we mortals, briefly and helplessly, live") and argues that time is a human convention derived from a space-time transformation by our nervous systems in which we have converted the motion of the earth around the sun into a repeating cycle by which we measure duration. The planetary system is seen as a giant clock used by us to express personal time.

The implications of Dr. Gooddy's position are many. He points out, for example, that the powerful reach their heights at about the same time that nervous decline is inevitable. He errs in suggesting that dementia is an obligatory part of aging, but his point that alterations in brain function are common in the elderly and that brain diseases are more common in this enlarging age group is well made. More concern about detecting these disorders in our growing gerontocracy is definitely warranted.

Dr. Gooddy provides many interesting insights in the course of his little book. For example, he observes that limb movements contribute to our sense of time. The vast majority of humans are between 5 and 6 feet tall and can walk several miles in one day. This common experience provides the basis of our most general and common-sense ideas of personal time. It also explains the experience of returning to one's childhood home to find that old haunts seem shrunken: our space-time determinants have changed with our increasing size. Likewise, he shows us that the routine medical and family histories are exercises in personal and transpersonal chronobiology, exploring time relationships of diseases as they evolve in individuals and families. Prognosis is a special form of forward vision in which predictions of events of future time is attempted. He discusses addiction and drug use as temporary escapes from time to provide an artificial elation "for the time being." He points out that alterations in the sense of personal time are important elements in many diseases, including mania, depression, schizophrenia, delirium, and dementia. With these observations he allows us to see our everyday clinical functions in a new and interesting light.

This is not an easy book. The concepts are difficult and the prose is often opaque. Nevertheless, Dr. Gooddy has cultured an unusual point of view in the course of a long and distinguished career in neurology, and he has achieved important insights. We can thank him for sharing them with us.

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The Bridge Between Neurology and Psychiatry, *edited by E.H. Reynolds, M.D., F.R.C.P., F.R.C.Psych., and M.R. Trimble, F.R.C.P., F.R.C.Psych. New York, Churchill Livingstone, 1989, 397 pp., $59.00.*

This volume is a memorial to Sir Denis Hill by his friends, colleagues, and admirers. The title of this book comes from a lecture by Sir Denis given at Birmingham, England, on the 50th anniversary of the foundation of the Birmingham Nerve Hospital. The lecture, chapter three of this volume, outlines the history of ideas in neurology and psychiatry and lays the groundwork for the remainder of the book. It should be required reading for any student of either discipline.

The essays are written by a list of authors that constitutes a "Who's Who" in neuropsychiatry: D. Frank Benson, R.H. Cawley, A.H. Crisp, John Cutting, George W. Fenton, Peter Fenwick, W.A. Lishman, C. David Marsden, Robin M. Murray, M.J. Owen, J. Oxbury, S. Oxbury, Michael A. Reveley, E.H. Reynolds, M. Rossor, Sir Martin Roth, Brian Kenneth Toone, Michael R. Trimble, and Stephen A. Whatley.

This book does not purport to be a textbook of psychiatry, and it is not a "how to do it" book. It does not replace Lishman's text *Organic Psychiatry* (1) or *The American Psychiatric Press Textbook of Neuropsychiatry* of Hales and Yudofsky (2). Through a series of elegant essays on topics including the classic challenges of neuropsychiatry, such as hysteria, states of consciousness, sleep, and disorders of language, it outlines the frontiers of psychiatric research. There are excellent reviews of EEG (better than buying a textbook), psychiatric genetics, neurotransmitters, and epilepsy. The dyscontrol syndrome is discussed, as are the many interfaces or "bridges" between neurology and psychiatry that are becoming apparent with the advances of neurophysiology, neuropathology, neuropharmacology, and the functional brain imaging procedures—magnetic resonance imaging, positron emission tomography, and computed EEG. Much new research is presented, and the essay format permits the authors to express more opinion and more discussion than would the usual journal article.

The real value of the book, however, is not the many excellent surveys of various aspects of neurology and psychiatry and their interaction but in what it reveals of the philosophy of being a physician. The approach to the patient as a suffering human being rather than an organism divided into subspecialties comes through in the various approaches presented to clinical problems. The complicated questions of mind versus body and free will versus determinism and the very foundations of historical Western thought are played out in the insightful reviews by this panel of experts. This is no mere compendium of treatments or theories but a good starting point for a discussion of what a curriculum in psychiatry ought to include. The advances in neuroscience may be among the most important in history but are in no way separate from the advances in immunology, molecular genetics, and cellular physiology common to other disciplines of medicine.

This book emphasizes the unity of medical treatment rather than the fragmentation that has most unfortunately separated neurology and psychiatry in the recent past. The bridge referred to in the title is in fact the underlying scientific basis of medical practice. The authors of this volume amply convey the excitement and rewards of patient care and the scientific search for the origins of the human mind.

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Neuropsychology, Neuropsychiatry, and Behavioral Neurology, *by Rhawn Joseph. New York, Plenum, 1990, 372 pp., $45.00.*

The Critical Issues in Neuropsychology series from Plenum Press, edited by A.E. Puente and C.R. Reynolds, includes primarily edited works thematically organized around important neuropsychological themes. In *Neuropsychology, Neuropsychiatry, and Behavioral Neurology,* the series moves to a more sweeping panorama: a tour de force by a single author that summarizes and synthesizes what is known of links between brain and behavior. In 372 densely written and extensively referenced pages, the reader may peer into the universe of what is known about the neurological determinants of thought, consciousness, emotion, and the unconscious.

The book is actually presented in two parts, although they are not demarcated as such. The first consists of the initial seven chapters, which are organized neuroanatomically according to cerebral hemispheric structures (i.e., frontal lobes, occipital lobes). This is the larger part of the book and is by far the more useful, original, and effective. These chapters offer more than traditional, "bullet-wound" neuropsychology, although they include reviews of the older "lesion-makes-deficit" research. There is a much greater sensitivity to the organismic interrelatedness of the brain here. Rhawn Joseph pays careful attention to current knowledge of neuroanatomical connections, especially intrahemispheric short- and intermediate-length association tracts. Some neurophysiology is also reviewed, and the reader has a glimpse of the fantastic electric choreography that is at work in the brain, cutting across our clumsy categories of lobes and layers. Important older literature is described, such as the contribution of Freedman and Watts concerning frontal lobe surgery and personality. Freud and the unconscious find their places as well in the chapters discussing contributions of limbic system and right hemisphere structures to noncognitive mental life. These seven chapters enliven neuropsychology and make the book worth its price for anyone with serious clinical or research interests in this field.

The last three chapters shift the focus of the book from anatomical regions to pathophysiologies: trauma, stroke, and tumor. These fields prove too broad even for someone with the considerable talents and experience demonstrated by the author, however. The descriptions of disease mechanisms, physiological processes, and clinical syndromes become more truncated here, as the book reaches beyond its behavioral expertise. These chapters might have been left out without harm to the excellent core of the book.

My conclusion is that *Neuropsychology, Neuropsychiatry, and Behavioral Neurology* is a brilliant review of major neuropsychological realms, placing them creatively in a neurological context. The three chapters at the end are not necessary for the impact of the work. Serious neuropsychological clinicians or academicians should have some familiarity with this book.

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DEMENTIA

Aging Brain and Dementia: New Trends in Diagnosis and Therapy, *edited by Leontino Battistin and Franz Gerstenbrand. New York, Alan R. Liss, 1990, 622 pp., $140.00.*

This volume, number 54 in the Neurology and Neurobiology series, is a collection of papers originally presented at a symposium on dementia held in Italy in September 1988. As may be expected from a collection of proceedings, the quality varies considerably from contribution to contribution and there are redundancies. As if to emphasize the heterogenous nature of the contributions, the manuscripts were apparently photocopied directly so that the print of each chapter differs from the next, which is most disconcerting to the reader.

The purpose of the conference was to present up-to-date information on the epidemiology and neurobiology of dementia as well as new trends in diagnosis. As such, this volume will be of interest only to researchers in dementia and geriatric psychiatrists with a particular focus on dementing illness. It is not for the average clinician.

Several chapters may be singled out as particularly useful. There is an excellent review of epidemiologic studies of Alzheimer's disease as well as the genetics of this disorder. Several contributors describe the neuropathology and clinical presentation of dementias associated with vascular disease and Parkinson's disease. There is a particularly useful review of normal age-related changes in the microscopic anatomy, protein metabolism, and neurotransmitter function of the brain.

Several chapters review the effects of neurotransmitter precursors and compounds that purport to stimulate aminergic as well as cholinergic neurotransmitter function. Much of this information has been presented in one form or another previously, but the overall reviews are useful. The most interesting new information gathered in this volume concerns the use of imaging techniques in the normal aging brain and in dementias of various etiologies. One contributor correlates brain electrical mapping information with magnetic resonance imaging and single photon emission computed tomography imaging and concludes that these three techniques together are useful in subclassifying dementias of different etiology.

The volume concludes with a presentation regarding a substance known as acetyl-L-carnitine, a naturally occurring substance in the human body that has some cholinergic properties. When given to patients with degenerative or vascular pathology, it induced some improvement in performance, suggesting that further study of this interesting substance would be exciting.

Unlike many collections of presented papers, this volume contains an outstanding index, which should make it especially useful for the researcher.

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Huntington's Disease: A Disorder of Families, *by Susan E. Folstein, M.D. Baltimore, The Johns Hopkins University Press, 1989, 224 pp., $40.00.*

Reading this book made me reflect on the status of psychiatry and on whether as psychiatrists we are where we want to be. It was no easy task to review this volume because I must admit that during most of my career I have had an orientation and bias very similar to the author's concerning the role of psychiatry in understanding neuropsychiatric disease. This "neuroscientific" viewpoint, in essence, craves validation of psychiatric principles outside of the field of psychiatry itself and posits that it is quite impossible to make a real contribution if one is *just* a psychiatrist. In certain academic circles, therefore, it is now quite fashionable for psychiatrists to have expertise in such diverse clinical fields as neurology, psychology, internal medicine, radiology, or even such basic disciplines as biochemistry, molecular biology, pharmacology, or physics. Are psychiatrists really able adequately to master more than their own specialty? Is there truly such little substance to psychiatry? One wonders whether the cost of multispecialization is a lack of sophistication in one's own field.

This book begins with a journeyman's chapter on the history of Huntington's disease, followed by chapters on the motor abnormalities, the dementia, and the emotional features of this disorder. The second section comprises chapters on clinical and basic research findings in the areas of neuropathology, neuroscience, epidemiology, and genetics. Third, there are chapters on the issues of diagnosis and care. The case examples that accompany each chapter are well chosen and effectively convey the clinical features the author is attempting to describe. I found the appendixes of this book particularly useful in that they constitute a guide to clinical assessment instruments used by the author in her research program; genealogical strategies for developing large kindreds; service organizations and agencies that a researcher, clinician, or patient might find useful; and the basics of genetic counseling. Finally, there is a comprehensive reference list of articles published in the last decade.

The author states in the preface that in the course of "facilitating the participation of patients in research," she has "become involved in many [Huntington's disease] research projects in psychology, neurology, genetics, pathology, and neuroscience, as well as in psychiatry . . . [her] primary interest." However, I do not know whether I like the end product of this style of scholarship. This book tries to span too much territory and hence comes up lacking in depth of understanding. It is unclear to me whether this volume is intended for psychiatrists, neurologists, psychologists, social workers, or the educated layman who is at risk for or suffering from Huntington's disease. Sections of the book that describe the neurology of Huntington's disease are geared to psychiatrists but are insufficient for neurologists; the psychiatric aspects are superficial but probably adequate for nonpsychiatrists; and the parts on basic science are meant to be understandable to clinicians.

This book may well help clinical researchers involved in developing a multidisciplinary program to study any of a variety of neuropsychiatric illnesses. However, an important lesson to be learned from this volume is that there is a real danger for such a researcher to become a manager, rather than a doer, of research with superficial involvement in several areas that are not psychiatry.

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Alzheimer's Disease: Advances in Neurology, vol. 51, *edited by Richard J. Wurtman, Suzanne Corkin, John H. Growdon, and Eva Ritter-Walker. New York, Raven Press, 1989, 310 pp., $85.00.*

This work reviews the current status of research on Alzheimer's disease. Workers in this area need to run fast to keep up with rapidly advancing knowledge in the field. This book provides a nice update that can be useful for clinician and researcher alike. There are five major topic areas: clinical and epidemiologic issues, pathology, neurochemistry, genetics and molecular biology, and, finally, treatment aspects.

The articles in the section on clinical diagnosis and epidemiology develop a useful cross-cultural perspective. These articles provide North American researchers with the perspective of our European colleagues. Of note is that although there is no European consensus about diagnostic criteria for Alzheimer's disease, a group called EURAGE is attempting to develop collaborative studies and criteria for entry into studies. The articles in this section are of use in that they are a directory of those doing research in Alzheimer's disease in Europe and provide useful contacts for researchers in the United States.

An article of particular interest is that of Jorm, who describes some interesting pitfalls of data analysis of Alzheimer's disease studies. Jorm adds some new insights in this paper, but I missed reference to his previous work on the pitfalls of subtyping, although these issues are raised by other authors in this section. These papers are required reading for those who wish to speak intelligently about subtyping of Alzheimer's disease.

Now well-armed to critique studies of subtyping of Alzheimer's disease, the editors launch into the section on studies of pathology and subtyping. If one carefully reads the first section on pitfalls of data analysis, the studies in this section provide interesting insights on how investigators try to produce high-quality research in the real world. The articles cover the "hot" issues in the area, including Lewy body dementia and parkinsonian symptoms, Binswanger's disease and white matter changes, and frontal lobe syndromes. These articles are quite complementary to the articles in the first section.

The third section discusses neurochemical and neurotransmitter issues. This section revolves around the cholinergic hypothesis, although most of the other concepts are discussed. It is quite appropriate to discuss this area in depth given the ongoing studies of tacrine (tetrahydroaminoacridine). Updates of most of the other theories of the molecular biology and genetics of Alzheimer's disease are discussed in section four. Articles include updates on neurofibrillary tangles, amyloid, amyloid precursors, and genetic linkage studies.

The last section discusses behavioral and treatment issues. There is a brief but concise review by Crook on memory changes in normal aging followed by discussion of the Baltimore Longitudinal Study of Aging by Arenberg and a review of drugs with potential effects on normal memory by Crook. These works provide good source materials for those unfamiliar with the field of normal aging research and complement the studies of pathological aging, i.e., Alzheimer's disease. Finally, there are detailed discussions of the various agents potentially of use in Alzheimer's disease, especially tacrine.

All in all, I found this book useful as a current review of the area. The articles are not so technical that one new to the field would feel lost. Yet there is enough material of sophistication for the researcher to find this a useful compendium.

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TEXTBOOKS

Clinical and Diagnostic Interviewing, *edited by Robert J. Craig, Ph.D. Northvale, N.J., Jason Aronson, 1989, 344 pp., $40.00.*

To prepare for this review, I asked 10 of my second-year medical students what the most important diagnostic tool in psychiatry was. After several votes for CT scan, magnetic resonance imaging, and EEG and one for positron emission tomography, a woman whose father is a psychoanalyst, looking anxious about the group's response, suggested the mental status examination. If a new book on clinical interviewing helps make that lone voice grow stronger, then bravo! The authors in this volume are committed to the idea that the clinical interview has specific technical aspects and has utility in the diagnosis of mental illness today. With that said, this book becomes a useful manual to explore the concepts and contexts, both physical and theoretical, of the interview.

In the introduction, Dr. Craig, the editor, makes it clear that few guidelines were imposed on his contributors to allow for the greatest possibility of teaching with a creative approach to the subject. His strategy has been successful, and what emerges is a compendium of complementary rather than conflicting material. The first portion of the book explores the settings of the clinical interview and a phenomenological orientation to the interview. The authors discuss patients' and therapists' expectations and the role of clinical judgment. These discussions are especially well done for the student, and I have used chapters from the book to teach medical students. The second part is geared more toward residents in psychiatry or psychology trainees. Sullivanian psychoanalytic and humanistic approaches to the interview are elaborated. From reading these chapters, one gets a clearer view of how information is elicited depending on one's theoretical persuasion.

The third part is written for those who want an in-depth view of techniques for interviewing patients with specific psychopathologies. It is, I feel, the least useful part of the book for the fully trained and the most useful for the beginner. It helps with questions students often ask, such as, What do I ask an alcoholic? How do I elicit psychosis? What's important in the forensic interview? What's important in the child evaluation?

Finally, the book contains information on focused interviews. The chapter on the mental status examination provides a useful view of the dynamic facets of this interview without ignoring the importance of assessing for organic etiologies. A discussion of the *DSM-III-R* multiaxial diagnostic system would have been useful here, and I feel the lack of such discussion limits the overall usefulness of the book for general psychiatry residents, who will have to find this vital information elsewhere. I am somewhat disappointed that a chapter on *DSM-III-R* was not included in what is an almost complete volume on interviewing techniques and the process of gathering and understanding clinical data in an interview.

In all, *Clinical and Diagnostic Interviewing* is a clinically useful book for practitioners in a wide variety of mental health specialties at different levels of training.

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Human Behavior: An Introduction for Medical Students, *edited by Alan Stoudemire, M.D. Philadelphia, J.B. Lippincott Co., 1990, 362 pp., $15.95 (paper).*

In the preface of this intriguing book, the editor tells us, "The primary emphasis . . . in medical training is devoted to assimilating a scientific knowledge base and practicing the technical aspects of medical diagnosis and treatment. Relatively little consistent attention is given to acquiring and developing the necessary knowledge and skills to understand and attend to the psychological and emotional needs of the medically ill" (p. xiii). Thus, the book attempts to give the biopsychosocial model both theoretical respectability and practical applicability. The goal is formidable indeed because it attempts to fill a gap in the current trends of medical education, almost blinded by the return of psychiatry to the "mainstream of medicine"—a good excuse for those who overtly or covertly advocate narrowness in the training of physicians. Furthermore, the book serves as the basis for the companion text in this series, *Clinical Psychiatry for Medical Students* (1) and, as such, reaffirms throughout its pages the unique dimension of any "basic science" for psychiatry.

The book has five sections and 13 chapters. As a good example of the complexity of most of the topics, chapter one, "The Biopsychosocial Model in Medical Practice," is, in reality, three chapters devoted to conceptual clarifications, epidemiology of psychiatric disorders in general medical practice, and concepts of social epidemiology and illness behavior, respectively. Although one gets the impression that a "humanistic approach" is considered similar to a "biopsychosocial approach," the case study ends up like a listing of independent variables, the psychological ones remaining exclusively at the descriptive level. The definitions of disease and illness may be questionable (2), and the concept of illness behavior, even though sanctioned by Kleinman, seems to be a catchall statement.

In chapter two, "Culture, Ethnicity, and Behavior and the Practice of Medicine," the question of whether some components of this volume are general articles or book chapters suddenly becomes relevant. Without any previous mention of *DSM-III-R,* the chapter includes it (p. 35) as a concept that, one presumes, the authors think should be familiar to the medical student. This chapter includes some commonplaces of the behavioral literature but also has a good review of sociology and the dangers of stereotyping. The assertion, however, that "the role of social class in determining behavior is closely intertwined with ethnicity" (p. 37) is questionable for precisely the same reasons that make the terms "social" and "cultural" different, in spite of their conventional linkage.

In section two, Two Fundamental Psychological Theories of Human Behavior, the two theories included are, predictably, psychoanalytic psychology (chapter three) and behavioral and social learning psychology (chapter four). Both chapters have excellent glossaries of key concepts. The chapter on psychoanalysis attempts to depict Freud as a champion of the biopsychosocial model, deemphasizing his excessive psychologism. Furthermore, it attempts to explore, in my opinion wrongly, the value of psychoanalysis as a theory of human behavior and a method of treatment, bypassing the fundamental aspect of psychoanalysis as a method of investigation of the mind. In fact, to include the study of psychoanalysis as a method of treatment is completely out of phase with the book's stated focus on the *medically* ill. It is, however, a good review, and I particularly liked the section on separation-individuation. The review on classical and operant conditioning and the contributions of the cognitivists are strengths of the chapter on behavioral psychology, even though the therapies read like a cookbook.

Not surprisingly, section three, Human Development, has the most chapters (five). This section is a good example of how clinical findings precede research on normality or, at least, enhance it substantially. The chapter sequence is quite appropriate. Chapter six, "Childhood and Adolescent Development," follows the approach of Gesell et al., avoids more or less successfully the risks of duplication, presents a very useful table on the correspondence of the stages of development according to different schools of thought, but cites an author (Tanner) nowhere to be found in the bibliography and implies that alterations in levels of steroid hormones are primarily responsible for birth defects and complications of pregnancy and delivery in mothers under emotional stress (p. 138).

Chapter seven, "Adult Development," is one of the best of the book and not only because this topic has not been explored in similar textbooks. It includes useful definitions and, predictably, uses Eriksonian concepts. The authors give over a total of seven pages to their introduction before entering into the subject matter—a tribute to its complexity. Another excellent chapter is "The Family in Human Development and Medical Practice." Although it discusses therapy without first outlining the pathology, it has extremely useful concepts of the family's basic functions and schools of family therapy. Its most original contribution, however, is the genogram, a drawing of a family tree that records important information for at least two or three generations. Although at an early stage in its development, this concept could open a very useful way to approach history taking in a manner reminiscent of the legacy of Adolf Meyer (3).

From chapter nine on, the book turns primarily biological. The titles are self-explanatory: "The Behavioral and Psychobiologic Effects of Developmental Trauma," "Ethology and Human Behavior," "Neurobiologic Aspects of Behavior," and "Behavioral Genetics." Whether this is homage to the "golden age of neuroscience" or the unspoken need to be scientific, all of these chapters obviously depart from the overall biopsychosocial philosophy. Neuronal group selection, ethological phenomena, neurotransmitters, and some of the recent genetic contributions to the etiopathogenesis of psychiatric conditions are very well presented.

The last chapter, the only one in the last section (Clinical Applications), deals with the supportive psychological care of the medically ill and presents excellent diagrams of abnormal illness responses and illness dynamics. In short, this is the best effort at conceptual integration in the whole volume.

It is precisely the attempt at a true integration that generates undue expectations of this book (4). The results fall short of such objective, not because of lack of skills or brilliance in the many distinguished contributors, but primarily because the model itself has not solved the problem of its intrinsic fragmentation, and its ubiquitous umbrella-like perspective is devoid of solid practical applicability, still running the risk of detours, repetitions, and cliché-like statements. Although some medical students are going to find very useful and clear definitions in this book, its overall goal—the excellent, integrated, and compassionate treatment of each patient as a unique individual—remains somewhat elusive. Several chapters present excellent case studies, the annotated bibliographies are quite thorough, and the information included in the appendix section is worthwhile. One hopes that the application of a problem-oriented method of teaching human behavior will be productive and result in the increase of psychiatric vocations. In the last analysis, however, the message of a book like this should be the solid appreciation by nonpsychiatric physicians of the documented value of the biological, psychological, and social views of the drama of human illness.

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RENATO D. ALARCON, M.D., M.P.H.
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Basic Child Psychiatry, 5th ed., *by Philip Barker, M.B., B.S., F.R.C.P.(Ed), F.R.C.P.(C), D.P.M., D.C.H. Cambridge, Mass., Blackwell Scientific (St. Louis, Mo., Mosby-Year Book, distributor), 1988, 399 pp., $53.00; $29.50 (paper).*

Knowledge in the field of child and adolescent psychiatry continues to grow. Although comprehensive textbooks provide detailed reviews, there is a need for an introductory text that could be used by a variety of health professionals at various levels of education. Philip Barker indicates, in his introduction, that the purpose of his most recent textbook is "to provide the newcomer to the field with the basic facts of the subject and information about where to learn more." Barker's book clearly achieves this goal.

The initial chapters present information about the development and diagnostic assessment of children and their families. Chapters that follow review major syndromes in child psychiatry, forensic psychiatry, abuse and neglect, and, finally, treatment and prevention. Chapters are concise and well organized. The typical chapter framework includes definition of the problem and issues, reports on the prevalence, and a list of hypotheses, and a brief section on treatment and outcome. Separate chapters are devoted to more in-depth discussions of psychiatric treatment of children.

Barker provides a review of therapies, including individual, family, group, and behavioral approaches and hypnotherapy. Other treatments include day-patient, inpatient, alternative family, educational remediation, and speech therapy. Unfortunately, the section on pharmacology is weaker in substance than those on other topics. For example, in the treatment of attention-deficit hyperactivity disorder, scant mention is made of the role of tricyclic antidepressant medication, an important pharmacological intervention. The reader wanting more information on pharmacotherapy is appropriately directed toward referenced material.

Dr. Barker's writing style leads to a very pleasant and quick read. Although the text is more than 350 pages long, it can be read from cover to cover in a relatively short time, lending itself to medical student rotations.

As intended, this clearly written and well-balanced text provides the basic facts of child and adolescent psychiatry; further, it supplies the reader with a comprehensive list of references. A variety of health professionals, including medical students and psychiatry residents, will find this book useful.

BRENT LOVETT, M.D.
GARY R. GAFFNEY, M.D.
Kansas City, Kan.

American Psychiatric Press Review of Psychiatry, vol. 9, *edited by Allan Tasman, M.D., Stephen M. Goldfinger, M.D., and Charles A. Kaufmann, M.D. Washington, D.C., American Psychiatric Press, 1990, 699 pp., $54.95.*

Like its predecessors, volume 9 of this annual review presents five topics in separate sections. Overall, the volume is a good one. Some of the sections, however, are plagued by careless editing, ranging from missing lines and misspellings (bupropion suddenly becomes buproprion throughout one chapter, and the incorrect form appears in the index), to self-contradictory or meaningless statements. It is hard to believe that the following sentence could have escaped any copyreader's attention: "In the face of such common, benign, but very rare, idiosyncratic reactions, this investigator suggests occasional initial blood count monitoring" (p. 182).

A review the length of this one cannot pretend to do justice to the good points of each section. At best, I can mention my favorites, with some indication of why they appealed. One recommended chapter is "Potential New Pharmacotherapies for Refractory Depression" by William Potter, Matthew Rudorfer, and Husseini Manji. It deals with classes of drugs whose mechanisms of action are distinct from those of the traditional tricyclics and monoamine oxidase inhibitors. Also interesting is chapter seven, "Sleep Restriction, Exercise, and Bright Lights: Alternative Therapies for Depression" by Eva Hillman, Daniel Kripke, and J. Christian Gillin.

Burton Reifler and Kimberly Sherrill, in "Dementias: Reversible and Irreversible," correctly denounce the overuse and misinterpretation of the concept of pseudodementia. They then discuss the treatable aspects of irreversibly demented patients (depression, drug toxicity, behavioral problems) and give due attention to "the second patient," the caregivers (usually family members) who overextend themselves and then fall prey to guilt or resentment.

Outstanding are chapters 16 and 17: "Development of Psychoanalytic Psychology: A Historical-Conceptual Overview," by Paul Ornstein and Jerald Kay, and "The Process of Psychoanalytic Psychotherapy: A Self-Psychological Perspective," by Anna Ornstein and Paul Ornstein. These chapters provide the most readable and understandable summary of Kohut's psychology and treatment approach that I have encountered.

In "Psychiatric Consultation to Oncology," Marguerite Lederberg, Mary Jane Massie, and Jimmie Holland discuss patient complaints that are dismissed as "just psychological" by the medical staff. They also deal with cancer pain management, the ethical issues and emotional reactions affecting medical decisions in the terminal care period, and alternative cancer therapies. Another excellent review in this section is chapter 24, "Psychiatric Consultation to Internal Medicine" by Alan Stoudemire and James Levenson.

Section five, AIDS and HIV Infections, edited by Stephen Goldfinger and Carolyn Robinowitz, is well edited, so there are none of the redundancies among chapters that occur in some of the other sections. In chapter 28, John Markowitz and Samuel Perry present a succinct medical overview of AIDS, and in chapter 29 Alexandra Beckett does the same for HIV-related nervous system disorders. "Public Policy, Legal, and Ethical Issues" are the focus of chapter 32 by James Krajeski. Public health measures, how policy decisions are made, HIV antibody testing and contact tracing, confidentiality, the duty to protect, and the obligation to treat are among the subjects presented, not to give dogmatic answers but to pose the relevant questions.

ROBERT J. CAMPBELL, M.D.
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CHILDREN AND FAMILIES

The Child's World of Illness: The Development of Health and Illness Behaviour, *by Simon R. Wilkinson. New York, Cambridge University Press, 1988, 288 pp., $52.50.*

Although the literature on consultation work with adults has expanded considerably in recent years, a similar growth has not yet occurred in child and adolescent psychiatry. This is particularly surprising because child psychiatry has its origins, in part, in pediatrics and because pediatric consultation continues to be a central aspect of child psychiatry training and practice. Given the potential importance of childhood illness on later illness and behavior, the relative dearth of literature in the area is unfortunate; it reflects a lack of research and researchers, the complications posed by considerations of developmental change, and a relative overemphasis on disease-specific, as opposed to more general, processes. Volumes like this one are, accordingly, particularly welcome.

This book draws heavily on concepts derived from the behavioral sciences in helping us understand how children understand and communicate their experience of illness. Although many concepts and terms will be somewhat unfamiliar to the clinician, the straightforward presentation and organization make for a highly readable book. The volume examines the development of children's concepts of illness and how these concepts are related to the broader social context of children's experience. For example, children's understanding of the contributions of dirt and germs and personal responsibility to illness are discussed. Interview data are used to illustrate developmental aspects of notions of illness and health. Additional chapters focus on the role of "pretend" illness in development of somatoform complaints and on implications of the author's model for consultation and health education. The emphasis on communication in all its myriad forms—through play, for example—provides an overarching framework that helps the reader place the volume within a broader context.

This volume will be particularly helpful for clinicians and trainees interested in improving their skills in consultation work. It is not a simple "how to" manual; rather, it provides an important and general approach to understanding, and facilitating, communication about illness and health. It should be of interest to those of us interested in better understanding a child's experience of illness and in communicating with children about such experiences.

FRED R. VOLKMAR, M.D.
New Haven, Conn.

Women in Families: A Framework for Family Therapy, *edited by Monica McGoldrick, Carol M. Anderson, and Froma Walsh. New York, W.W. Norton & Co., 1989, 479 pp., $34.95.*

In the last 3 years, four important books have been published that examine, criticize, and propose innovations in family therapy from a feminist perspective. Like other forms of psychotherapy, family therapy has ignored or underestimated the importance of gender. Two of these books focus primarily on how to practice family and couples therapy that has been informed by feminism, one by a group of younger women therapists (1) and the other by a more experienced group of therapists from the Ackerman Institute (2). In addition, Deborah Luepnitz (3) has published a critical feminist evaluation of the major theories used by family therapists, which she supplements by some case reports of her own work. Finally, there is the book being reviewed here. It is a multiauthored collection of papers written, for the most part, specifically for this volume and supplemented by a few classical papers from the literature. Each of these books has a different flavor and offers the reader different opportunities to rethink his or her theories, to learn, and to become a better therapist.

All of these books place gender at the very center of their theorizing, research, and practice. In this regard, these authors are different from the pioneers in family therapy, who either ignored gender or who had a patriarchal bias. These authors differ as well from the systemic family therapists, who have tended to treat all members of the family as abstract "punctuations" in an informational network of mutual influence and thereby ignored differences in power. They also take issue with structural family therapists, who have viewed the family in functional terms (it looks this way because this way works), and the problem-focused family therapists, who wanted to alleviate ("solve") the problem regardless of the injustices inherent in the allocation of gender responsibilities. With gender as a loadstone, attention is drawn to the inherent inequality and unfairness of much of family life: to issues of power, mother blaming, the abuse of wives, the relative impoverishment of women and children after divorce, and the effects of a social system that removes men from families, leaves the children to the care of overburdened women, and then holds the women responsible for the children's problems.

This book does not focus attention on any one of these issues; rather, it discusses all of them and many more. At the outset, it should be said that this is an excellent collection of papers, and, of course, like all collections, some of the papers were more interesting than others. I found the following particularly useful: Walsh and Scheinkman's chapter, "(Fe)male: The Hidden Gender Dimension in Models of Family Therapy," Goldner's "Generation and Gender: Normative and Covert Hierarchies," Hare-Mustin's classic and pioneering "The Problem of Gender in Family Therapy," Taggart's "Epistemological Equality as the Fulfillment of Family Therapy," and McGoldrick's "Women Through the Family Life Cycle." This outline will also serve to give the reader a flavor of the book.

Certain other chapters on specific issues deserve special comment. Roth's chapter on psychotherapy with lesbian couples will be useful to anyone working with this population and, in addition, sheds light on relational problems more generally. Anderson and Holder have written an excellent, brief, but comprehensive overview of the special presentations and problems of the female mental patient. Laird, who discusses the importance of stories in how we understand life, emphasizes a therapeutic avenue often overlooked. Although it is, unfortunately, commonly believed that working with the woman in an addictive couple is a way of holding her responsible, and although it can be, Bepko clearly demonstrates that, if practiced responsibly, it can be an effective method of empowering women. This chapter also demonstrates that the person with whom one works in psychotherapy is less important than the goals of that work, whether to hold responsible and blame or to understand and empower. There is no reason why one cannot understand and empower more than one person at a time. This is an unfortunate dichotomy around which family therapy and feminist therapists have become polarized.

Reading the whole book leaves one with the impression that there is somewhat too much overlap and that it has, perhaps, too sociological a perspective. On the other hand, it is useful to be reminded of the many ways in which women are disadvantaged—economically, socially, psychiatrically, culturally, and by many social systems. It is true that class, race, and gender often overlap.

What was missing for this male reader was the opportunity to read about women's unique inner experience of marital and family life. Almost certainly men would not share their inner experiences in an edited volume. Braverman, alone, describes enough about her relationship with her mother and her own children to make her chapter, "Beyond the Myth of Motherhood," personally involving. Perhaps we become therapists in part because we want to listen to stories; certainly we hear enough of them. Braverman's story highlights both the lies in the myth of motherhood and the truths it contains, which the rest of her chapter discusses. But perhaps I am asking too much of an excellent volume that I can only encourage others to buy and read.

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HENRY GRUNEBAUM, M.D.
Cambridge, Mass.

Family Transitions: Continuity and Change Over the Life Cycle, *edited by Celia Jaes Falicov. New York, Guilford Press, 1989, 486 pp., $35.00.*

Falicov and her collaborators have produced a fine book, one with many contributions that advance the field of family therapy. Like all collections, however, some pieces are outstanding and others restate familiar positions, some are ambitious and others are pedestrian, and some succeed and others do not. However, more than many books, this volume is an effort to go beyond where we are now. It attempts a new synthesis using the concept of family transitions in family life and in therapy as the focal point. A caveat is in order because the field of family therapy is small and I know and am friendly with several of the contributors.

The single most outstanding contribution in this book is by the editor. Her chapter is a thoughtful and clear effort to integrate the various conceptions of family transitions and development and to locate the different approaches to family therapy in relation to these concepts. She goes beyond the boundaries of family therapy to discuss sociology, she endeavors and, to some extent, succeeds in integrating a life cycle approach with systems theory, and she is both inclusive and incisive. This piece of work sets an unusually high standard for the book as a whole.

Other outstanding chapters that deserve special mention are those by Wynne, who describes an epigenetic model of family processes; Bennett, Wolin, and McAvity, who discuss the relationship among family identity, rituals, and myths; and Liddle, whose chapter is entitled "Developmental Thinking and the Family Life Cycle: Implications for Training Family Therapists." Many of the other pieces in this book will also be quite useful to clinicians and teachers. One more essay that deserves special comment is that by Joselevich, an Argentine family therapist, who beautifully describes the treatment of a family transition involving cumulative stress and crises.

There are many other good pieces of work in this volume and also a few that either do not bear on the subject or are poorly thought out. One reviews this volume with admiration for the editor, her courage, and her high goals but wishes that all of her collaborators had been able to live up to the intellectual challenge of her ideals. This is an ambitious work well worth owning and reading selectively.

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Reprints of Book Forum reviews are not available.

Letters to the Editor

Comments on the Klerman-Stone Debate on *Osheroff v. Chestnut Lodge*

SIR: Apparently, Gerald L. Klerman, M.D.'s thoughtful presentation "The Psychiatric Patient's Right to Effective Treatment: Implications of *Osheroff v. Chestnut Lodge*" (1) is, in the 1990s, still a subject for debate by a prominent psychoanalyst. This is not surprising in view of the schools-of-thought syndrome that still bedevils our field of psychiatry.

After a critical reading of Dr. Klerman's argument, I wondered who would have the temerity to write in opposition. The rebuttal by Alan A. Stone, M.D. (2) may well be the best case a clever man can make, if he is willing to redefine the argument and present himself as an attorney for the defense. I quote: "The principal inquiry to be considered here, therefore, is how Klerman's paper would be understood by a lawyer contemplating a malpractice suit against a psychoanalytically oriented psychiatrist" (p. 419).

Whereas Dr. Klerman appeals to psychiatrists to use scientific methodology in their clinical work, Dr. Stone, in his remarks, shows his lack of understanding. Use of the word "oriented," although it was popular during my residency and fellowship years, suggests a biased psychiatrist to competent attorneys. Sounding to me like an attorney with a weak case, Dr. Stone argues, "Much of what all physicians do has no demonstrated effectiveness—even the prescription of supposedly efficacious medication" (p. 424). Just how uninformed and gullible does he think his readers are?

Dr. Stone shamefully, in my view, chose to distort some aspects of Dr. Klerman's paper so that he could then easily knock these straw men down. I'll leave it to Dr. Klerman to clarify.

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PAUL L. KINGSLEY, M.D.
Ross, Calif.

SIR: As pointed out by Dr. Stone in the landmark debate with Dr. Klerman, hazardous risks of malpractice lie in store for all psychiatrists who fail to diagnose and treat depressed patients in accordance with psychopharmacological standards of care. Dr. Klerman asserts that a psychiatrist has the responsibility to make a proper diagnosis in accordance with *DSM-III-R* criteria. I dare say that Dr. Klerman knows that *DSM-III-R* is an atheoretical classification of mental disorders and makes no claim about causes of mental disorders. Without knowledge of etiology and given the abstract nature of functional mental disorders, there can only be opinions about diagnosis. On the basis of information provided by both authors, Chestnut Lodge's evaluation that Dr. Osheroff's diagnosis was narcissistic personality disorder stands on as firm ground as does Silver Hill Foundation's diagnosis of major depression with psychotic features. What Silver Hill Foundation saw as psychotic symptoms could have been seen by Chestnut Lodge as histrionic symptoms. There is overlap between narcissistic and histrionic personality disorder. What one psychiatrist perceives as psychotic hallucinations is seen by another as hysterical hallucinations (conversion disorder).

Plaintiff attorneys zealously seek out experts like Dr. Klerman who have the authority to convince a jury that causality exists, whereas all that might be true is the association of unrelated phenomena. Thus, the administration of antidepressive and antipsychotic drugs concurrently with the psychodynamic changes that occurred when Dr. Osheroff moved from one hospital to another (including change of treaters and, as pointed out by Dr. Stone, the triumph or vindication over negative transference to the degree of being able to file a potentially successful lawsuit) confound any claim that it was the dramatic effects of medication which cured the patient in 3 short weeks!

With regard to Dr. Klerman's claim that psychopharmacological treatment is subject to proof of efficacy through drug-controlled studies, whereas psychoanalysis is not, I refer him to an editorial in the *New England Journal of Medicine* concerning economic incentives in clinical investigation (1). It is common knowledge that drug-manufacturing companies spend millions of dollars researching psychopharmacological agents, and there is considerable pressure, unconscious if not conscious, on researchers to produce findings favoring efficacy of a drug. This explains, to a large extent, why in the true testing ground of clinical practice we find that the drugs are not always what the research studies imply they are supposed to be.

I need hardly remind Dr. Klerman that psychopharmacological treatment, like psychotherapy, remains empirical. The use of an antidepressant that elevates amines in the CNS together with an antipsychotic that reduces dopamine in the CNS is not accepted by all psychiatrists as being acceptable pharmacological management. This practice might represent polypharmacy, where one drug neutralizes the effects of the other.

Despite the advances in neuroscience over the past decade, psychiatry remains an infant science, at the same time representing the most global level at which the art of medicine is practiced. A discipline that currently relies more on art than science should not invoke empirical standards of care but rely on ordinary standards in accordance with the truth of the state of knowledge of our profession.

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THEODORE PEARLMAN, M.D.
Houston, Tex.

SIR: Dr. Alan Stone's paper goes to the heart of the issue facing psychiatry today. Are psychoanalysis and medical psychiatry compatible? Dr. Stone refers to himself as a classical psychiatrist. I was trained before psychoanalysis triumphed and never could accept psychoanalysis. I consider myself a classical psychiatrist; the current changes indicate a return to the prepsychoanalysis traditions. Psychoanalysis had an answer for everything, and the analyst saw himself as all-wise. It was very seductive in its promises.

I believe that psychiatry and psychoanalysis must come to a parting of the ways. Psychiatry can no longer accept different theories as simple differences of opinion. Any theory, to be taken seriously and supported, must obey the laws of science. Freud felt that psychoanalysis was not a medical discipline. For once I agree with him.

As a profession we still imply support for nonefficacious therapies that are justified by theory only. This is especially pervasive in child psychiatry. The longer we defend psychoanalysis, the less believable we will become.

HANS R. HUESSY, M.D.
Burlington, Vt.

SIR: Reading the debate on *Osheroff v. Chestnut Lodge* was like inhaling a breath of fresh air after reading so many articles in the *Journal* that deal with statistical correlations between some chemical substance and some constellation of symptoms. Such articles are obviously important; they just happen to be boring. Hence, it was refreshing to read a debate that had considerable spunk on both sides.

I think the polarization of psychiatry into biological and psychotherapy factions need not be so pronounced. It is certainly common to see patients who respond to pharmacotherapy when they have not responded to psychotherapy. It is also common to see a patient who has been interviewed with a simplistic symptom checklist and then given one antidepressant after another, when whether or not the patient is feeling mirrored or abandoned is of much greater importance to his clinical status than is his antidepressant medication. The difficulty is that mirroring and abandonment issues cannot be measured as easily as sleep and appetite disturbances. This does not mean that such issues are not real; they just cannot be measured by objective means.

As with most such disagreements, both biological psychiatrists (even though they like to pride themselves on being objective scientists) and psychoanalysts see what they want to see. Why not use both pharmacotherapy and psychotherapy approaches in helping patients? Why does it have to be one or the other?

RONALD TASKA, M.D.
Durham, N.C.

SIR: Although the history of Chestnut Lodge is intertwined with psychodynamic psychiatry in the United States through the writings of Sullivan, Fromm-Reichmann, Searles, Stanton, and others, readers of the recent debate may be left with the impression that Chestnut Lodge is suspended in an ideological time capsule. Accordingly, a brief but current view of the hospital's clinical and research activities may be in order.

Chestnut Lodge provides specialized care for patients with psychotic conditions and severe personality disorders who have not improved or have deteriorated despite multiple inpatient and outpatient treatment efforts. In addition to pharmacotherapy and the more traditional modalities such as group or individual psychotherapy, the treatment program for psychotic disorders may include participation in a token economy, social skills training, and a variety of prevocational and other rehabilitative activities. In 1987 the hospital was the first in the Washington area to use clozapine on an experimental basis. Over one-half of our severely and chronically ill patients reside in the community, participating in a comprehensive support program that includes supervised housing, a day hospital, 24-hour crisis intervention, and, often, competitive employment through a work adjustment program that takes advantage of the healthy local economy.

Consistent with advancing knowledge over the past decade, greater emphasis is placed on the role of comorbid axis 1 disorders, cognitive dysfunction, and genetic predisposition in the evaluation and treatment of severe personality disorders. When patients' previous noncompliance with attempted pharmacological interventions has precluded an assessment of their usefulness, medication trials in a controlled setting can offer a major advantage (1). Resulting improvements in cognitive efficiency or affective stability may facilitate intensive psychotherapy, which aims at identifying and correcting repetitive dysfunctional interpersonal and behavioral patterns that are the defining features of personality disorders.

Our aim is to treat but also to study. For example, how can we understand those who inexplicably resist, refuse, or fail to respond to pharmacological therapy? While these problems have been studied from a psychodynamic standpoint, institutional and collaborative research efforts have also included studies of illness heterogeneity (W.S. Fenton and T.H. McGlashan, manuscript submitted for publication, 1990) and the possible role of viral infections in the etiology of schizophrenia (2). An ongoing collaborative investigation with the National Institute of Mental Health explores comorbidity and the neurobiology of severe personality disorders.

Dr. Klerman and associates' description of inconsistent use of medication in his own hospital in 1979 (3) demonstrates the rapid evolution of standards of care as we learn more about the neurobiological underpinnings and psychosocial determinants of severe mental disorders. In the 1990s, his quixotic quest to slay the "psychodynamic purist" is dated. If Dr. Stone is correct, however, this crusade could become an inquisition, an effort to press an idiosyncratic agenda with stifling implications for scientific practice and clinical innovation. Dr. Klerman's moral quilt is sewn with an Orwellian stitch, replete with dramatic rhetoric and inarguable slogans. We are disturbed by his exploitation of *Osheroff* and casting of Chestnut Lodge as a symbol of an antiquated and dilapidated psychodynamic psychiatry. This bears little relation to current reality.

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WAYNE S. FENTON, M.D.
THOMAS H. MCGLASHAN, M.D.
Rockville, Md.

SIR: Dr. Klerman has arrived at sweeping conclusions and recommendations on the basis of his subjective analysis of a single case. Surely this form of generalization violates the boundaries of scientific validity that he purports to uphold. I offer a brief case vignette to develop this point further.

> Ms. A, a 58-year-old woman, was referred for ongoing treatment of chronic depression. For the previous 8 years she had been under the care of the psychopharmacology service of a community hospital. During this time she had had trials of therapeutic doses of several different antidepressants and medication combinations, with mild to moderate clinical response. The incompleteness of her response was attested to by the number of different therapeutic trials. At one point she had experienced obvious clinical deterioration based on an idealized, eroticized transference reaction to a male resident who had been briefly involved in her care. This had been dealt with by neuropsychiatric investigation, which yielded normal results.
>
> On assessment Ms. A described a number of sources of unresolved resentment in her life, including marital dissatisfaction, childhood deprivation, and difficulty forming intimate relationships. A course of psychodynamic psychotherapy was undertaken. After several months Ms. A improved remarkably, to the point where medication was no longer required, and she began to experience fulfillment in a variety of areas.

It would be absurd to use the case of Ms. A to condemn the entire field of psychopharmacology. Like Dr. Osheroff, Ms. A suffered from the lack of a comprehensive biopsychosocial approach (1) by those charged with her care. In both cases there occurred an excessive adherence to a single form of treatment without adequate consideration of alternative or adjunctive therapies. The implementation of Dr. Klerman's recommendations can only serve to exacerbate such narrow-mindedness and to deprive our patients of the individualized case formulation and treatment that they require.

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JACK KLEIN, M.D., D.PSYCH.
Ottawa, Ont., Canada

SIR: We recently published a book (1) reviewing the empirical evidence on biological treatments for psychological distress and comparing the results to those obtained with psychotherapy and placebo. We were, therefore, quite interested in Dr. Klerman's article advocating a legal imperative for drug treatment of depression under the guise of "a right to effective treatment." The argument is based on the idea that for depression, drug treatments have been empirically validated as clearly effective and superior to the various forms of psychotherapy. While the goal of basing treatments on scientific findings is laudable, Dr. Klerman's conclusions go well beyond the current state of knowledge, minimize the leap from research to practice, and suggest a clarity of findings that, frankly, do not exist.

In our review of the evidence on antidepressants, we were repeatedly startled to see inconsistent interpretations of the same research findings by different writers. In truth, conclusions drawn about psychopharmacological outcome are more shaky than is typically acknowledged.

The research literature on the effectiveness of antidepressants is beset with methodological problems. For example, there is reason to believe that a sine qua non for unbiased drug research, the double-blind design, is a semifiction. Physicians giving the medications (and doing the outcome ratings) in these studies usually know who is getting the active drug and who is getting the inactive placebo (2). Their outcome ratings are therefore subject to bias. In studies using an active placebo control condition (which produces body sensations), differences between antidepressant and placebo in effectiveness shrivel (2). Similarly, the effectiveness of standard antidepressant drugs fades when they are embedded in studies comparing them to both newer antidepressant medications and placebo (2). Presumably, in this situation the researchers are not focused on trying to prove the efficacy of the older drugs, and the identification of the standard drug is more obscured by a design that includes a second active drug as well as a placebo.

As for comparisons with psychotherapy, Dr. Klerman again appears to overstate the case for antidepressants. Our review (2) showed that when a specified type of psychotherapy for depression (such as cognitive psychotherapy) was compared to drug treatment, it either surpassed the results with medication (five trials) or equaled the results with medication (three trials). None of the trials showed the drug to be superior. Adding drugs to psychotherapy also made no difference in treatment outcome in nine of 11 trials.

In sum, we feel that it would be more consonant with the evidence to keep treatment claims modest and to acknowledge the uncertainties that exist. At best, antidepressants may offer a unique solution for 20%–30% of treated cases. In view of the disparate interpretations of the drug outcome literature, as recently acknowledged by a panel of internationally eminent psychiatrists (3), it appears inappropriate to advocate a narrow, court-imposed standard for the treatment of depression. No one approach has as yet cornered the market on efficacy, and we need a continued flow of both data and debate.

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ROGER P. GREENBERG, PH.D.
SEYMOUR FISHER, PH.D.
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SIR: We are at present in a stage of natural transition from a more primitive to a more scientific method of treatment. Drs. Klerman and Stone represent different phases in the transition from psychodynamic to biological psychiatry. Dr. Klerman seems to have crossed over the dividing line, but Dr. Stone seems to be ambivalently treading on both sides of it. Dr. Klerman has successfully suppressed his dynamic orientation, whereas Dr. Stone's rationalization and intellectualization seem to protect him from the conflict of having to acknowledge changing times.

Before antibiotics, fevers were treated with different indigenous methods ranging from witch doctors to home remedies. The fever in most cases subsided not because of the treatment but because it had run its natural course. For a small proportion of patients, there was no cure until the advent of antibiotics. Similarly, in the field of mental illness, we are in a stage where we have found the medications for some mental illnesses without being able to pinpoint their real mode of action or specificity, not unlike the "shotgun treatment" era of antibiotic therapy.

Dr. Klerman deals with mental illness at a manifest level and resorts to biological treatment. Dr. Stone handles mental illness at an interpretive level. Even if it is agreed that all of our current behaviors are based on past experiences, in most instances these are uncorrelatable because of the magnitude of the past experiences. In interpretive therapy, efficacy depends on the patient. The passive and psychologically naive patient believes in any interpretation. In most instances there is no real cure. The patient is "cured" because the therapist says so. We also have the intellectual patient who actively absorbs the interpretation and later uses it in interpersonal communication.

Medicine in general in the past has been subjective, and this continues even today to an extent that is much greater in psychodynamic psychiatry than in other fields of medicine. Therefore, it is no wonder that traditionalists criticize the more objective *DSM-III-R*. Objectivity is the cornerstone for the advancement of any science, and *DSM-III-R* diagnoses help to maintain this objectivity. As physicians we have to be scientific; medicine is a science, and the most scientific at this time is the biological approach. The analytical approach may predict the patient's attitude and response to treatment and this would be useful, but most often it is an intellectual exercise that is ego-supportive not so much for the patient as for the therapist.

V. BHUJANG, M.D.
Detroit, Mich.

SIR: As the identified patient, I object to the diagnosis of narcissistic personality disorder put forth by Dr. Stone. Dr. Stone supports his inferences with a constricted, biased, and inaccurate database upon which he constructs his public assessment of my capacity for object relations.

Dr. Stone ascribes "conflicts" with associates to my alleged character pathology, whereas a nationally circulated magazine article (1) clearly delineates the contrary facts. Dr. Stone sees only grandiosity in my memoir, while others have found it a significant statement of the patient's viewpoint.

Dr. Stone opines that my prehospital drug treatment failed because of characterologically induced noncompliance. If that was the case, why didn't the hospital use the controlled environment to ensure compliance with the medication regimen? Similarly, he opines that my psychodynamic history conforms to Dr. Kernberg's description of the pattern of narcissistic personality. If so, then why wasn't I treated according to Dr. Kernberg's recommendations—i.e., when major depression occurs in a characterologically disordered patient, "the treatment of the psychosis must take precedence over the treatment of the personality disorder" (2). Dr. Kernberg further recommends treatment of the depression with drugs or ECT. Upon recovery from the depression, the patient resumes outpatient psychotherapy to treat the character pathology.

Dr. Stone asserts that my initial treatment plan was formulated specifically to deal with alleged pathological narcissism. In fact, the transcript of the treatment planning conference (held after 3 months of evaluation) makes no mention of personality disorder at all, nor do the billing forms submitted to my insurance company over a period of 7 months. There is, however, repetitive use of descriptors such as involutional melancholia, agitated melancholia, and agitated depression. Would Dr. Stone's traditional psychiatrist prescribe a Procrustean program now acknowledged by its proponents to be neither effective nor (as attested by a rather high incidence of suicide) safe (3–5)?

Dr. Stone fails to mention that over the last 10 years I have rebuilt my professional credibility and relationships with all my children and that I have married and functioned well in society and have prevailed in two highly prolonged and stressful litigations. Furthermore, I have never felt entitled to anything except safe and effective medical treatment.

On the basis of these considerations, I find Dr. Stone's statements to be more an attempt to undermine my credibility than a properly validated diagnosis. Psychiatric malpractice should not be obscured by a fictitious camouflage that conveniently manufactures differing "schools of thought" and attacks the plaintiff's character.

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RAPHAEL J. OSHEROFF, M.D.
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SIR: Dr. Stone's paper discussing *Osheroff v. Chestnut Lodge* was disturbing. The merits of psychodynamic treatment are not well illustrated by this case. Dr. Stone fears that Dr. Klerman's arguments "might . . . raise the specter of malpractice . . . for the majority of psychiatrists in the United States who . . . provide [traditional] treatments" (p. 426). However, it is unclear that Dr. Klerman's position would support such an extreme outcome or that traditional practitioners would be hurt by documentation of the efficacy of psychodynamic treatment, as Dr. Klerman advocates.

Dr. Stone indicates that he does not see Dr. Osheroff's case as one about which biological and traditional psychiatrists would disagree and insists that he would have treated this patient biologically. He further contends that the law's interference with biological treatment in such a situation would be tantamount to forcing the physician to commit malpractice. Therefore, his suggestion that "Dr. Osheroff was able to litigate because he was able to obtain expert witnesses like Klerman . . . willing to testify that there is a consensus about efficacious treatment" (p. 424) is puzzling. Does Dr. Stone think Dr. Klerman should not have agreed to testify? Or that no patient has the right to a successful malpractice case if the treating physician was practicing traditional psychiatry?

The issue in *Osheroff* is not whether it is malpractice to treat a patient with traditional psychotherapy, or even to do so exclusively, in the face of obvious clinical deterioration, as Dr. Stone states. It is that somatic treatments *of proven efficacy* were not used. A malpractice suit arguing that this patient should have been transferred to another hospital to facilitate a narcissistic triumph would have been unlikely, although Dr. Stone feels that this represents a likely mechanism for the patient's improvement.

Dr. Klerman would consider important the question of whether a psychoanalytic and/or a neurophysiologic mechanism best explains this patient's recovery. He would not suggest that traditional psychotherapy had no role in the treatment of this patient. Dr. Klerman is not an opponent of psychoanalysis. He is not interested in "controlling his colleagues," nor is he a proponent of "rigid orthodoxy," as Dr. Stone suggests (p. 425). The contention that psychopharmacologists "can take Klerman's paper as authority for the proposition that they need never discuss or refer a patient for traditional therapy, since such treatments have no demonstrated efficacy compared to their own" (p. 426) represents a logical fallacy and an unnecessarily provocative conclusion. Such an outcome would be far from Dr. Klerman's intent.

The substance and tone of Dr. Stone's paper contain a personal indictment of Dr. Klerman. This approach fails as a contribution to the crucially important dialogue between psychoanalysis and biological psychiatry, which needs to be facilitated by mutual respect rather than diverted by false accusation. It is also unfair to a highly distinguished colleague whose propositions should be used to encourage intellectual rigor in all we do, including traditional psychotherapy. Those of us who believe in the validity of psychoanalytic principles and the usefulness of psychodynamic psychotherapy need to collaborate with colleagues like Dr. Klerman. The question is not who wins the debate but, rather, how we can achieve productive integration of two separate and well-established trends in the profession.

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SIR: Dr. Stone's reply to Dr. Klerman's discussion of *Osheroff v. Chestnut Lodge* implies that he speaks for a unified position represented by psychoanalytic psychotherapists. This is hardly the case. There is great debate in psychoanalysis concerning the psychodynamics and psychotherapy of major depression, the subject of which I have addressed from the viewpoint of self psychology (1, 2).

Dr. Stone uses the details of Dr. Osheroff's clinical history to show that difficulties in professional and personal spheres had surfaced before his hospitalization. Dr. Stone calls these difficulties "conflicts"; his wording advances the theory that unresolved, unconscious intrapsychic conflict underlay the difficulties—an essential feature of classical psychoanalytic theory. Clinical data to support classical psychoanalytic theory have been generated and reported throughout the twentieth century, but only by therapists using the classical psychoanalytic situation in a narrow range of circumstances. Otherwise, the theory is unproven.

Dr. Stone's justification of the behavior of Chestnut Lodge is based on the thesis that treatment was attempting to address the patient's unconscious conflicts through the use of intensive individual psychodynamic psychotherapy and that a respectable minority of physicians would find such a treatment approach reasonable. Well before 1979, respected psychoanalysts (3) warned against the dangers inherent in ascribing to only one viewpoint.

By using solely the vantage point of unconscious conflict, one cannot consider how individual psychotherapy, in itself, may contribute to a depressed patient's disintegration. From this vantage point, one cannot consider that biologically inheritable, developmental, or acquired deficits in psychic structure and/or function underlie difficulties and depressive symptoms, a position that is just as reasonable (and for which there is considerable evidence in the psychiatric and psychoanalytic literature) as the unconscious conflict theory. And finally, from this narrow vantage point, one cannot consider the possibility that Dr. Osheroff's improvement at Silver Hill resulted from a psychotherapeutic stance that more appropriately addressed his needs, a stance acknowledging the legitimacy of pharmacotherapy in addressing a component of depression.

The reader of Dr. Stone's paper is left with the conclusion that all psychodynamically oriented therapists operate according to the unconscious intrapsychic conflict model of psychopathology and that Dr. Klerman is indicting all psychodynamic practitioners who would investigate the unconscious dimensions of the self. This is just not so.

Cognitive psychotherapy (4), interpersonal psychotherapy (5), and behavioral psychotherapy encourage awareness of unconscious aspects of "automatic" thoughts, feelings, behaviors, and attachments. Such awareness promotes development of skills conducive to the attainment and maintenance of more rewarding attachments and more adaptive behaviors. Any of these psychotherapies might have more appropriately addressed Dr. Osheroff's difficulties.

What disturbs this psychoanalytic psychiatrist is Dr. Stone's justification of the perseverance of the "respectable minority" treatment approach in the face of obvious deterioration in Dr. Osheroff's clinical status during treatment. Assuming that a negative response resulted from the treatment at Chestnut Lodge, why did it take 7 months to diagnose? Why weren't other psychotherapeutic approaches tried? Finally, why did others have to intervene on the patient's behalf to effect a transfer to a different environment? Dr. Stone's constituency must respond nondogmatically and directly to these questions. Until they do, traditional psychoanalysts will continue to lose the respect of their colleagues and patients. Now more than ever, the continuing progress in the battle to destigmatize mental illness requires forthright responses.

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Dr. Klerman Replies

SIR: I appreciate Dr. Kingsley's letter in support of my position. The majority of the letters were highly critical of me personally and often ad hominem. Dr. Kingsley understands my point of view and appears to accept it as his own.

Dr. Pearlman's comments about the state of psychopharmacology research and differences within the profession are interesting but hardly relevant to *Osheroff v. Chestnut Lodge*. There was little disagreement between staffs at Chestnut Lodge and at Silver Hill about the diagnosis of major depression with psychotic features. Dr. Pearlman invokes the possible diagnosis of histrionic personality, but there is no mention of that diagnosis in either the Silver Hill Foundation or the Chestnut Lodge records. Whatever the limitations of the psychopharmacological research literature, they are minor compared to the absence of a literature on the efficacy of psychodynamic psychotherapy, such as that which Dr. Osheroff received, for psychotic depression.

Dr. Huessy condemns psychoanalysis and believes that psychoanalysis and psychiatry should part. I believe that this parting would be a loss to both parties. Psychoanalysis has enriched American psychiatry in the past and has the capability to do so in the future. At the same time, I agree with Dr. Huessy that it is desirable that psychoanalysis obey the laws of science and also provide support for the efficacy of treatment. Hopefully, the winds of change in psychodynamic psychiatry will bring those changes about and allow psychodynamic psychiatry and psychoanalysis to become scientific and continue to enrich American psychiatry.

Dr. Taska raises a number of issues concerning the current state of biological and psychotherapy practice and research and identifies a number of unresolved methodologic and measurement issues. I agree that they merit further effort. He calls for increased use of combined pharmacotherapy and psychotherapy. Prescriptions for psychopharmacological agents are on the increase, as is patient utilization of psychotherapeutic services. Whether or not the combination of pharmacotherapy and psychotherapy is useful depends, in my opinion, on the individual case and the state of the scientific evidence for the treatment of the disorder from which the patient suffers. Just as I would not arbitrarily advocate pharmacotherapy or psychotherapy for every depression, I would not automatically advocate combination therapy as a way of promoting the rapprochement between psychodynamic psychiatry and biological psychiatry. The value of combined treatment needs to be determined for each individual disorder and by appropriately controlled trials.

I am pleased to learn that Chestnut Lodge has changed in the directions described by Drs. Fenton and McGlashan. From information from other sources, I have reason to agree that Chestnut Lodge today is not the same institution it was in 1979 when Dr. Osheroff was a patient. However, I was not pleased by the closing comments, which attack my sincerity and reasonableness. I am not involved in a "crusade" or "quixotic quest to slay the 'psychodynamic purist.'" While I do not consider myself a psychoanalyst, I have had psychoanalytic training at Boston and Western New England institutes and am an affiliate member of the Boston Psychoanalytic Society. My agenda is the enhancement of the scientific foundations of psychiatry, including psychodynamic psychiatry. Psychodynamic psychiatry in the 1960s and 1970s became doctrinaire and rigid. Drs. Fenton and McGlashan feel that my assessment of the scientific state of psychodynamic psychiatry is "dated"; that term acknowledges past difficulties of the type I wrote about. That Chestnut Lodge has changed is commendable, but episodes like Dr. Osheroff's case helped to stimulate that change. It would be far better if Drs. Fenton and McGlashan acknowledged that change has occurred without referring to my presentation as "replete with dramatic rhetoric and inarguable slogans." I don't know what those terms mean. What parts do they label as dramatic rhetoric? What terms are slogans? Attacks on my credibility only serve to obscure the issues and perpetuate discord.

I disagree with Dr. Klein's interpretation of my intentions. I did not intentionally undertake, nor do I believe I undertook, a condemnation of the entire field of psychoanalysis and psychodynamic psychiatry. I object to the characterization of my position by Dr. Stone as "an indictment of psychoanalytic psychiatry." I am critical of a number of aspects of contemporary psychodynamic psychiatry, particularly the failure to bring forth evidence for the efficacy of treatments. I am not proposing an exclusive adherence to a single form of treatment, i.e., medication. I have conducted research on psychotherapy, and to accuse me of narrow-mindedness is to ignore the bulk of my psychiatric career and the extensive research and writings on the treatment of depression by interpersonal psychotherapy (1).

It is obvious that Drs. Greenberg and Fisher draw more conclusions from the literature on clinical psychopharmacological trials than I do. Many individual psychopharmacological studies may well be deficient in specific methodologic and design matters. However, the whole body of studies on a given drug needs to be considered before coming to any conclusion. I conclude, as do the majority of clinicians and researchers, that tricyclics have statistically significant and clinically meaningful effects on depressive symptoms in the short run (6–20 weeks), and when maintained over long-term treatment (1–3 years), they prevent recurrence or relapse. Drs. Greenberg and Fisher seem unaware of the recent findings from the National Institute of Mental Health psychotherapy study reported by Elkin et al. (2) and the Pittsburgh studies reported by Frank et al. (3). What about a possible critique of psychotherapy research? Have Drs. Greenberg and Fisher applied their same methodologic scrutiny to psychotherapy studies? For example, they would find that the corpus of studies on cognitive behavioral therapy includes only two studies with placebo or other control. The reference to the Marks et al. letter is irrelevant, since it dealt with a study of benzodiazepines in patients with anxiety disorder. I am a strong advocate of psychotherapy for acute depressions (1). However, the form of psychotherapy provided for Dr. Osheroff at Chestnut Lodge (long-term individual psychodynamic psychotherapy) was not working after 6 months. There are no clinical studies of the efficacy of psychotherapy in hospitalized, psychotically depressed individuals. All the studies showing efficacy of psychotherapy have been done on ambulatory nonpsychotic patients whose illnesses were less severe than that of Dr. Osheroff.

Dr. Bhujang has an interesting view of change in contemporary psychiatry. He postulates a transition from a "primitive," "interpretive" psychiatry based on psychodynamic principles to biological psychiatry, which he regards as objective and scientific. He attributes a similar position to me: "Dr. Klerman has successfully suppressed his dynamic orientation." I would not accept that characterization of my position. My position is that it is true that there is tension between biological and psychodynamic psychiatry. At the current moment, biological psychiatry is more identified with scientific method and objective approaches to psychopathology such as *DSM-III*. However, in my opinion, there is no intrinsic reason why psychodynamic psychiatry cannot be scientific and make greater use of systematic observation, experimentation, and quantitative techniques. The fact that it has not become scientific is not, in my opinion, intrinsic to psychoanalysis but more reflective of the social organization of dynamic psychiatry and the values and orientations of the psychoanalytic institutes.

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GERALD L. KLERMAN, M.D.
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Dr. Stone Replies

SIR: Let me first thank all of those who have commented on this important discussion in these pages and in the many thoughtful personal communications. The subject obviously touches on our professional identity as both scientists and humanists. Unfortunately, the exchange between Dr. Klerman and myself has produced heat as well as light and, apparently, some misunderstanding.

Dr. Kingsley is one of several writers who apparently missed the basic point of the disagreement between Dr. Klerman and myself. If Dr. Klerman had confined himself to "appeals to psychiatrists to use scientific methodology in their clinical work" instead of discussing legal issues and suggesting standards of care that could be used for malpractice litigation, there would have been no need for a response from me. Unfortunately, he chose to make the *Osheroff* litigation the basis of his paper and to conflate his understanding of the case as an adversarial witness with science and policy.

Although I did not myself address the line of arguments made in Dr. Pearlman's letter, they are related to what I believe is a central issue in the debate, namely, how certain can we be about the scientific validity of existing efficacy research? Although Dr. Kingsley thinks that only gullible and uninformed readers would accept my questioning of that certainty, there are many quite sophisticated scientists who agree. I encourage him to read the articles cited in references 19 and 20 of my paper. The sentence beginning, "Much of what all physicians do," which Dr. Kingsley finds so outrageous, echoes the sentiments expressed by Relman in his *New England Journal of Medicine* editorial (reference 19). The methodological complexities of efficacy studies in psychiatry are demonstrated by the recent controversy among the experts about how to interpret the results of the NIMH collaborative study of the treatment of depression (1). There is, in addition, quite contradictory authority contesting Dr. Klerman's claims and guidelines for proper treatment (2).

Dr. Huessy has apparently confused the terms "classical" and "traditional." In writing my response, it felt awkward to string together repeatedly the words "psychoanalytic," "psychoanalytically oriented," and "psychodynamically oriented" psychiatry. The term "traditional" was offered as an appropriate catchall. It is regrettable that Dr. Huessy has had such an unpleasant experience with pretentious psychoanalysts, but I am sure he will agree that pretentiousness is not confined to that group.

Both Dr. Klerman and I agree with Dr. Taska. Our difference of opinion concerned the question of when and under what circumstances traditional psychotherapy alone becomes malpractice.

I deeply regret that in my effort to document the diagnosis of narcissistic personality disorder in his case, Dr. Osheroff feels I have undermined his credibility or attacked his character; that was not my intention. I am delighted that he has been able to rebuild his life. Beyond those matters, his letter emphasizes that Kernberg, whose work I quoted, recommends that when major depression occurs in a character-disordered patient, appropriate drugs or ECT should be used. I do not disagree with Dr. Kernberg's views. A fair reading of my response to Dr. Klerman should make that clear. Indeed, as I emphasized, even if the initial treatment plan in 1979 was appropriate, it eventually became clear that Dr. Osheroff had deteriorated and become psychotically depressed. At such a point it is the current consensus of American psychiatry that drugs or ECT should be used. Although there may be a respectable minority that disagrees, I am not a member of that minority group.

Dr. Shear, in her reading of my response to Dr. Klerman, recognizes that point, but she considers my response "disturbing." She finds much to criticize about my logic and about the tone of my paper. I disagree with all of her judgments, but I shall deal here with only one of them. She suggests that a malpractice suit arguing transfer "to another hospital to facilitate a narcissistic triumph" would have been unlikely to succeed. That is certainly true, but I would certainly never have proposed a lawsuit on that basis. What I did suggest was that a failure to obtain consultation in the face of serious psychotic deterioration and to initiate more appropriate treatment would be a departure from the standard of care. My comment about the effects of the transfer were obviously presented to suggest that Dr. Osheroff's dramatic and remarkable cure was in some significant measure to be understood in psychodynamic terms and could not be reduced to the magical efficacy of drugs. Dr. Shear does put an interesting question: Do I believe Dr. Klerman should "not have agreed to testify?" Elsewhere, I have discussed the ethical, moral, and scientific problems of psychiatric expert testimony. The unfortunate tendency in such expert testimony that I deplore is for the psychiatrist to express his or her views with unwarranted certitude and scientific authority. However, Dr. Klerman had every right to testify, as did all of the other experts. I would hope that in exercising this right, experts would not attempt to use the courts to impose a narrow or partisan perspective on their colleagues. It is this concern that motivated my effort to respond to Dr. Klerman.

Dr. Shear mentions the importance of mutual respect. Dr. Klerman and I have known each other since we were both candidates in the Boston Psychoanalytic Institute. I hope my response has not caused Dr. Klerman or anyone else to have any doubt about my respect for him.

Finally, Dr. Dietz's letter makes a point about his self psychology approach to psychodynamic therapy. Dr. Dietz's claim is that his *kind* of psychotherapy is different from the intrapsychic conflict *kind* used by Chestnut Lodge, which he infers that I endorse. Let me say that I am not the official or unofficial spokesperson for any kind of psychotherapy or for psychoanalysis. There are, of course, many approaches to psychotherapy and many minor and major variations. Almost none of these approaches has been subjected to the kind of efficacy study that Dr. Klerman argues is necessary. Unless Dr. Dietz has such data about his self psychology approach, he stands on no stronger ground by Dr. Klerman's criteria than do the other traditional psychotherapies based on opinion, theories, and collective experience. He is in the same boat at which the scientific efficacy study torpedoes are aimed. Dr. Klerman, however, believes there are sufficient data to demonstrate that his own approach of interpersonal psychotherapy is efficacious. Having familiarized myself with interpersonal psychotherapy, it seems to me to have many features similar to traditional psychodynamic therapy of the kind many eclectic psychiatrists practice and have practiced for decades. Similarly, many psychoanalytically oriented psychiatrists have been assimilating cognitive therapy, also supposedly efficacious. If psychotherapists can emphasize how much they have in common rather than stressing their differences, then perhaps it is possible to conclude that the broad spectrum of "traditional" psychiatrists practice a generic brand of psychotherapy that has, under different trade names, been found efficacious for certain *DSM-III-R* diagnoses. Although I write this in the hope of striking a humorous note, it is not meant as a facetious conclusion.

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ALAN A. STONE, M.D.
Cambridge, Mass.

Absence Seizures Induced by Lithium: Possible Interaction With Fluoxetine

SIR: Seizures associated with lithium treatment are rare at therapeutic plasma levels (0.5–1.5 meq/liter), especially in the absence of a previous history of epilepsy. Two cases of lithium-induced neurotoxicity have recently been published. In one case (1), addition of fluoxetine to the patient's treatment induced an elevation in serum lithium level to the toxic range. In the second (2), toxicity appeared when lithium was added to fluoxetine therapy, although the patient's serum lithium levels remained well within the therapeutic range. Two other cases of increased levels and manic episodes after the introduction of fluoxetine have been reported (3).

We present a case of absence seizures in a patient without a previous history of epilepsy that was possibly related to an interaction between lithium and fluoxetine.

> Mr. A, a 44-year-old patient with the diagnosis of major depressive disorder, had been treated with pirlindole (150 mg/day), prazepam (20 mg/day), and triazolam (0.25 mg/day). He had no personal or family history of epilepsy, as assessed later by a neurologist. Because of his inadequate response to these drugs, treatment with lithium was begun and then gradually increased from 600 to 1600 mg/day over 13 months. Coinciding with the increase in the daily dose of lithium to 1600 mg, all other drugs were withdrawn and fluoxetine, at a dose of 40 mg/day, was introduced. After 42 days, during which Mr. A's situation was stable, he was seen to become immobile and stare into space. This lasted for a few seconds, and then he began an activity different from the one he had been engaged in before the episode. He had no recollection of these events, which recurred twice in the following month. After the third such episode, the dose of lithium was reduced to 1200 mg/day, while the dose of fluoxetine remained unchanged. An EEG performed 5 days after the last episode was reported as showing no abnormality. Lithium levels before the first episode were within the therapeutic range, fluctuating between 0.6 and 0.9 meq/liter.

Although blood samples were not drawn during these episodes (they occurred in the patient's home), it is unlikely that these would have revealed a toxic lithium level, as all determinations during the previous months were well within the therapeutic range, and no change in the patient's life habits and medication (including over-the-counter drugs) could be identified. We feel that the episodes most probably were absences; however, no EEG recordings were made during the acute period, so it is possible that they were complex partial seizures.

We attributed the adverse reaction to lithium (or to a lithium-fluoxetine interaction) because the absences developed when the lithium dose was highest, disappeared when lithium was withdrawn, and did not recur when lithium was reintroduced at a lower dose, despite the continuation of fluoxetine treatment.

The pathophysiology of this apparent interaction is unknown. Francis and Traill (4) demonstrated that lithium is concentrated in CNS tissue, and Elizur et al. (5) suggested that CNS lithium concentrations would be better reflected by erythrocyte than by serum levels. Any factor raising the erythrocyte/plasma ratio could result in the development of CNS toxicity, even with therapeutic plasma levels. In the case of Mr. A, fluoxetine could have played such a role.

To the best of our knowledge, this is the first case of lithium-induced absence seizures in a patient without a history of epilepsy, as well as one of the first reports of a fluoxetine-lithium interaction. Since this combination of drugs may be used increasingly in the future, we think that patients receiving this treatment should be carefully monitored.

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A Case of Recurrent Premenstrual Psychosis

SIR: We read with interest the recent review of psychiatric syndromes linked to reproductive function (1) and would like to report a case of recurrent premenstrual psychosis probably related to an underlying seizure disorder. A brain electrical activity mapping (BEAM) study was used to clarify the diagnosis.

> Ms. A, a 35-year-old married woman, had suffered anxiety, irritability, and emotional lability during the week before her menses for 15 years. Eighteen months before her most recent admission to the hospital, she suffered a psychotic episode 10 days before her menses that was characterized by paranoia, auditory hallucinations, and violent outbursts. She was hospitalized and placed on a regimen of trifluoperazine, and all symptoms cleared when her menses occurred. During the following 8 months, she developed psychotic symptoms before her menses and they cleared when her menses appeared; four times she required hospitalization. Her symptoms included paranoid delusions, auditory hallucinations, and marked ideas of reference from television. Evaluation during hospitalization, which included urine drug screen, CBC, thyroid function tests, CT scan of the head, antinuclear antibody and electrolyte levels, EEG, and neurologic examination, produced unremarkable results. There was no history of psychiatric illness or convulsions. Ms. A was given trials of antipsychotics, antidepressants, birth control pills, and pyridoxine without success. Her family reported stereotypic behavior during the episodes: repeated hand clapping, turning the shower on and off, blank staring, and blinking. A diagnosis of obsessive-compulsive disorder was entertained. Eight months before the recent admission, a BEAM study revealed a right temporal-occipital abnormality suggestive of a seizure focus. Ms. A was begun on a regimen of carbamazepine, maintained at a level of 8–10 μg/ml, and all premenstrual symptoms cleared until the current admission.
>
> The week prior to admission, Ms. A began a new job and slept little. She believed that her coworkers and psychiatrist were plotting against her; she heard voices from her car radio. Her husband reported lip smacking, staring spells, and undirected violence. On admission her serum carbamazepine level was 5.5 μg/ml; her serum prolactin level was 79 ng/ml. She was not taking neuroleptics. All other laboratory data and results of a physical examination were normal. Her symptoms resolved in 2 days with the onset of her menses, and her prolactin level fell to 15 ng/ml. A neurology consultant concurred with the diagnosis of complex partial seizures.

The patient's premenstrual symptoms—initially anxiety and finally psychosis—likely reflected paroxysmal limbic activity, although the ictal state was difficult to detect. The BEAM study alerted us to the stereotypy, and the elevated prolactin levels suggested the diagnosis of complex partial seizures. The primary symptoms were behavioral and difficult to recognize as ictus-related.

This case was probably an unusual form of catamenial epilepsy, because of the peri-ictal psychosis and the consistent relation with the menses. The relation between seizures and menses is unclear, although water metabolism and endocrine changes are suspected factors (2). Ms. A's psychotic relapse after 8 symptom-free months probably was due to sleep deprivation and a subtherapeutic carbamazepine blood level. That is, this psychosis was secondary to breakthrough seizure activity. We wonder, as Price (3) did, whether the perimenstrual psychosis described by Endo et al. (4) reflected a subtle underlying limbic ictal focus. Although BEAM is a controversial instrument (5), in this puzzling case it led to proper diagnosis and treatment. Temporal lobe epilepsy should be considered an uncommon reason for premenstrual behavioral disturbances.

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Iron Overload in Psychiatric Illness

SIR: Little emphasis has been placed in the psychiatric and other medical literature on the psychiatric manifestations of iron overload. Niederau et al. (1) found neurological manifestations such as depression, lethargy, and disorientation in several patients with hereditary hemochromatosis. Dementia and ataxia have been reported as presenting symptoms of hereditary hemochromatosis (2), and a disabling fatigue has been reported to be the most common symptom; it has been reported in over 80% of patients at the time of diagnosis (1).

Following the conclusion of Fairbanks and Baldus in 1986 (3) that iron overload was more common than realized—and missed too frequently—I began to look at iron metabolism in patients with resistant psychiatric syndromes. I found seven patients who had either clinical evidence of hereditary hemochromatosis (i.e., skin bronzing, hepatosplenomegaly) or laboratory evidence of hereditary hemochromatosis (i.e., elevated serum iron or transferrin saturation index or positive urinary challenge to the iron chelator deferoxamine. In all seven of these patients no disorder of iron metabolism had been previously considered. My treatment consisted of twice weekly injections of deferoxamine, 10 mg/kg i.m., until iron parameters and clinical abnormalities had returned to normal. I have seen significant clinical improvements in resistant anxiety, depression, obsessions, compulsions, and panic attacks in these patients. They have been followed for months with no regression.

Iron plays a key role in many brain enzymes, specifically, tyrosine hydroxylase, monoamine oxidase, and phenylalanine hydroxylase (4). Thus, psychiatric manifestations of iron overload should not be unexpected. The amount of storage iron (ferritin) in the CNS is larger than realized, i.e., 30% of that found in the liver, which is considered the major storage site of iron. Unfortunately, we have been misled into thinking that hereditary hemochromatosis is rare, and we do not yet think of iron overload as a somatic factor in the etiology of psychiatric illness. Hereditary hemochromatosis is the most common autosomal recessive inborn error of metabolism; 0.3% of the white population are true homozygotes, and 15.0% of the white population are heterozygotes or carriers.

I have found the use of deferoxamine a very safe and useful adjunct in the treatment of patients with varying psychiatric manifestations due to hereditary hemochromatosis. I (5) and others have now published articles on the safe use of deferoxamine to correct iron overload in other conditions.

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Low Serum Iron Levels and Neuroleptic Malignant Syndrome

SIR: We were interested in the findings of Patricia Rosebush, M.Sc.N., M.D., and Thomas Stewart, M.D., in their article on neuroleptic malignant syndrome (1). They reported that nearly all the patients they studied were agitated and restless before developing neuroleptic malignant syndrome, and they questioned whether this represented undiagnosed akathisia, which may have created a state-dependent predisposition to neuroleptic malignant syndrome. They also found that 95% of their subjects had low serum iron levels, although it was unclear whether this predated the development of neuroleptic malignant syndrome.

A previous report of ours (2) may be relevant in this matter and tie these two findings together. We found that subjects with akathisia had significantly lower serum iron levels than matched control subjects. There is evidence that iron modulates dopamine D_2 receptor function, as iron is known to constitute part of this receptor (3). Iron-deficient rats have decreased numbers of D_2 receptors and reduced behavioral responses to apomorphine, amphetamine, and opioids (4). We proposed that the low serum iron level, through an induced D_2 receptor hypofunction, increases the susceptibility to akathisia in patients taking antipsychotic medication.

Although the pathophysiology of neuroleptic malignant syndrome is not clear, there is general agreement that D_2 receptor blockade is implicated (5). It is possible that preexisting low serum iron levels would predispose to this by causing reduced numbers and impaired function of D_2 receptors.

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Dr. Rosebush and Dr. Mazurek Reply

SIR: We appreciate the comments by Drs. White and Brown suggesting that the low serum iron levels found in our study of patients with neuroleptic malignant syndrome may be linked to the motor restlessness which predated the neuroleptic malignant syndrome in most of our cases. In view of their finding that serum iron levels are low in many cases of akathisia, they have wondered whether the patients in our series may have had preexisting low levels of serum iron that predisposed them to neuroleptic malignant syndrome. We have some further data that may help clarify this issue.

The serum iron values (N=19) reported in our article represented the lowest level measured during each individual episode of neuroleptic malignant syndrome. We have now studied serum iron in 25 cases of neuroleptic malignant syndrome and are fortunate enough to have, for six of our cases, serum iron determinations that predated the onset of neuroleptic malignant syndrome.

In these six cases the serum iron fell precipitously from mean±SD levels of 85±29 μg/dl before neuroleptic malignant syndrome to 35±17 μg/dl with the onset of the syndrome. This represented a mean±SD drop of 60%±14% (range=37%–81%) (Rosebush and Mazurek, unpublished data). These data, which were not included in our original article, suggest that the extremely low serum iron levels found during neuroleptic malignant syndrome do not precede the episode but, rather, are specific to the disorder itself.

Another point worth mentioning is that akathisia is a common complication of neuroleptic therapy, occurring in at least 20% of neuroleptic-treated psychiatric patients (1, 2). Neuroleptic malignant syndrome, on the other hand, is a rare event, and has been estimated to occur in 0.07% (3) to 1.4% (4) of hospitalized patients exposed to neuroleptics.

It is our hypothesis that the low serum iron levels found in neuroleptic malignant syndrome may indeed participate in the pathophysiology of the disorder. Rather than seeing low levels of serum iron as predisposing to neuroleptic malignant syndrome, however, we think that the available data favor there being some other initiating factor which induces a dramatic drop in serum iron at the onset of neuroleptic malignant syndrome. This sudden decrease of serum iron may then in turn contribute to the clinical presentation of neuroleptic malignant syndrome by interfering with dopamine D_2 receptor function (5).

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Hypothesis About Borderline Personality Disorder

Sir: I am writing in reference to the article "Perceptions of Parental Bonding in Borderline Patients" by Joel Paris, M.D., and Hallie Frank, Ph.D. (1), which is a good addition to the literature on borderline patients. However, I disagree with the authors' choosing the neglect hypothesis rather than the overprotection hypothesis of the development of borderline personality disorder. The data they presented, with the exception of the paper by Gunderson et al. (2), do not really lend themselves to supporting the neglect hypothesis. The study by Gunderson et al. was the only one in which the parents were interviewed; all of the authors' papers and most of the others they cited were based on information from the patients. Obviously, these are biased data. The borderline patients of the present, much like the hysterical patients of Zetzel (3) in the past, are well-known for distorting data and for initially trying to please the therapist. Data coming from these patients, therefore, should always be suspect unless they can be validated by other, more neutral sources.

Still, one is left to try to make sense of the neglect hypothesis, which is put forth consistently (and most intensely) by borderline patients. My hypothesis is that it is both true and not true at the same time. It is based in the pleasure principle (4), and as we are all aware, pleasure and pain are relative. My theory is that borderline patients, during the first year of their lives, are overprotected and overgratified. Then, as they reach the separation and individuation phase (5), instinctual gratification becomes more sophisticated, and also reality begins to have an effect upon their world. The overgratifying mother is no longer capable (or willing) to *fully* gratify the instinctual demands of this child who is a future borderline patient. The perception of the child, therefore, is one of acute deprivation as contrasted to the previous overgratification. It is the combination of this overgratification and then abrupt perceived deprivation that probably fixates the child at this particular psychosexual level of development. Of course, fixation at this level carries along with it all of the other types of problems, such as immature defenses, narcissistic object relationships, and preverbal communication style.

Perhaps someone will wish to set up a study to see if this hypothesis can be proved or disproved.

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Dr. Paris and Dr. Frank Reply

Sir: We have already acknowledged in our article that borderline patients can retrospectively distort their childhood experiences. The theory proposed by Dr. Knoll resembles that of Masterson and Rinsley (1) but is not readily open to empirical investigation. The only conceivable way to test it would be to carry out longitudinal follow-up of infants exposed to different patterns of mothering, and this is unlikely to be practical.

The idea that infancy and early childhood are crucial in the development of abnormal personality is an aspect of psychoanalytic theory for which there is at present no existing empirical support. In fact, there is a wide body of research evidence supporting the view that adult psychopathology results from the cumulative effects of many environmental traumas over the course of childhood interacting with constitutional vulnerabilities (2). The advantage of the instrument used in our study, Parker et al.'s Parental Bonding Instrument (3), is that it deals with childhood as a whole and with recoverable memories.

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Effects of Gun Laws on Suicide Rates

Sir: The article by Charles L. Rich, M.D., and associates suggesting that some substitution of suicide method occurred after the city of Toronto enacted a sweeping gun ban (1) reports one of the most convincing studies to date on this issue. However, because the authors' examination of the rate of suicide by various methods in the city lacked a breakdown by age or sex of the victims, it must be assumed that there was stability in these statistics during the study years. Although a recent study in Vancouver (2) reached the similar conclusion that gun laws did not reduce the overall suicide rate, it demonstrated a reduction in the suicide rate in the 15- to 24-year-old age group, indicating the need to use statistics that are method-specific for age and sex.

Also pertinent to the findings of Dr. Rich and associates is a study conducted in Ontario that examined a variety of factors in suicides and attempted suicides among persons 15–24 years of age during 1971–1978, before the ban on guns (3). It found firearm suicides to be 12 times more common by males than by females, while jumping deaths were only twice as frequent. However, there was a diminishing influence of sex on the choice of method as increasing numbers of women chose violent means.

Dr. Rich and associates did not rule out age-related effects, and they did report in their San Diego data that most men under 30 years old who had committed suicide with a gun had had no prior psychiatric treatment, while the majority of those in the older age group had histories of psychiatric hospitalization. This agrees with the characterization of youths who commit suicide as impulsive in nature, which may explain why they may be less likely to turn to another method when they are unable to obtain a firearm (2).

The Ontario study (3) also demonstrated a significant difference in method between suicides in rural and urban areas; suicides in the rural areas generally involved guns because they were more widely available, whereas victims in cities chose jumping predominantly because of the presence of subways, bridges, tall buildings, and moving automobiles. Because the effect of changes in the availability or toxicity of a suicide method will largely depend on the frequency of its use, some change to a more prevalent method such as jumping should not have been so unexpected when guns were banned in the city of Toronto. The possibility that some victims came into the city to carry out their jumping suicides cannot be completely ruled out either.

Gun control laws cannot have as great an effect on preventing suicides as they are likely to have on reducing firearm homicides. In a violent culture such as ours, however, making a distinction between deaths that are suicides and those that are homicides is often difficult, since the latter may represent an element of risk-taking and be self-inflicted to a degree. If we do not make any effort to control the spread of guns, it will only be giving further sanction to the use of violence, which is already endemic in our society.

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ROBERT EILERS, M.D.
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Dr. Rich Replies

SIR: Dr. Eilers' points are well made. He describes, as we attempted to do, some of the great number of mostly uncontrollable variables involved in such naturalistic observations. Like Dr. Eilers, we also called for further systematic investigation of the issue. I personally do not usually have much difficulty in differentiating the intent to die of the person who commits suicide from the lack of such intent in homicides. On the other hand, it seems inescapable to conclude that guns play a role in a good many American homicides. The political problem of gun control in the United States is well-known. Our major clinical point, however, was and remains that suicidal individuals—be they old or young, urban or rural—cannot be considered out of harm's way simply because they do not have access to a gun.

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Reprints of letters to the Editor are not available.

THE AMERICAN JOURNAL OF PSYCHIATRY

Editorial

The APA Task Force Report on Benzodiazepine Dependence, Toxicity, and Abuse

In 1987 the American Psychiatric Association, recognizing the need for guidelines for prescribing benzodiazepines, established a task force to gather and report on the available information regarding these widely prescribed drugs. The report has recently been published by APA (1) and is strongly recommended to all psychiatrists. The report represents a group consensus; agreement was not unanimous on all points. The work of the task force was supported entirely by APA funding.

Although many adults may take an occasional benzodiazepine, two-thirds of therapeutic use is for 60 days or less. Small but substantial numbers of adults have been taking benzodiazepines daily (or nightly) for 1 year or more. Over a period of many years, these adults represent 1.65% of the population, and they fall into four distinct groups. The first group comprises older, medically ill patients who are taking other medications. Benzodiazepines are usually prescribed for these patients by a nonpsychiatrist. The second group comprises psychiatric patients with panic or agoraphobic disorders. In the first and second groups, benzodiazepines are seldom abused, doses are not escalated, and patients as well as their physicians attest to the therapeutic necessity for the medication. The third group comprises psychiatric and general medical patients with recurrent dysphoria. Because of the vagueness and chronicity of symptoms in this group, the indications for long-term use are less certain than those for the first two groups. Occasional patients may escalate their doses, and abuse of higher doses in combination with alcohol or other abused substances may occur. The fourth group is composed of patients with chronic sleep disorder. Although research data do not consistently support the long-term hypnotic efficacy of benzodiazepines when taken for more than 30 consecutive nights, some patients claim that they cannot sleep without a benzodiazepine at bedtime. To what extent regular nightly benzodiazepines are preventing rebound insomnia or actually are treating a chronic sleep disturbance is not known.

Therapeutic use of benzodiazepines can be associated with potential hazards to the patient. True physical dependence can arise from chronic therapeutic use, defined by the appearance of a constellation of discontinuance symptoms following abrupt withdrawal. These symptoms can be divided into three categories: rebound, recurrence, and withdrawal. Rebound symptoms, the first to appear after drug termination, are the mirror image of the effects of the drug (worse anxiety, insomnia, and restlessness) and may be severe enough to cause the patient to return to the drug. For some short-half-life benzodiazepines, rebound symptoms may appear between doses, so that patients become dependent and are aware when the next dose will be needed. Other discontinuance symptoms, usually appearing after rebound, may be identical to the symptoms for which the drug was originally prescribed and confuse both the patient and the clinician. It is often difficult to determine whether these symptoms represent a recurrence of the original reasons for the benzodiazepine prescription, a manifestation of drug discontinuance, or both. Withdrawal symptoms that were not present when the drug was initially prescribed make up the third category of discontinuance symptoms. Seizures and psychosis are infrequent but are the most serious of the withdrawal symptoms. They occur after high doses, long duration of treatment, and abrupt discontinuation, and the risk of seizures may be higher when another drug that lowers the seizure threshold is also being used. Other disconcerting withdrawal symptoms include tinnitus, depression, and a sensation of seasickness. Although all discontinuance symptoms occur primarily after abrupt drug termination, they may also appear after gradual tapering, especially in patients who have been taking higher than usual doses or have been taking therapeutic doses for extended periods of time.

The types of discontinuance symptoms are the same for both long- and short-half-life benzodiazepines. Clinical experience suggests, however, that short-half-life benzodiazepines, especially those which also have high potency, produce a more severe discontinuance syndrome that appears earlier than with long-half-life drugs. The severity of these discontinuance symptoms is reduced when doses are very slowly tapered. Clinical experience also suggests that high-potency, short-half-life benzodiazepines are more likely than other benzodiazepines to induce a state of therapeutic dose dependence, although there are no research data to confirm these observations.

In young and middle-aged adults, benzodiazepine toxicity is usually mild unless the drug is mixed with other sedative hypnotics or alcohol. Sedation, unsteadiness, and impaired psychomotor speed and accuracy are well-known benzodiazepine effects. Driving skills are not usually impaired by regular therapeutic doses of benzodiazepines but may be substantially compromised when a benzodiazepine is mixed with alcohol or when it is taken by a benzodiazepine-naive person. Clinicians should regularly warn their patients about the risks of driving while taking benzodiazepines, and the mixing of alcohol or other sedative hypnotics must be forbidden if the patient is to drive.

Among the elderly, the toxicity of benzodiazepines takes on an additional dimension. Subtle but measurable cognitive impairment may be associated with both acute and chronic therapeutic doses of benzodiazepines. Unsteadiness and an increased predisposition to falling are not uncommon, so that extra caution must be exercised when benzodiazepines are prescribed.

In summary, benzodiazepines are important therapeutic drugs when carefully prescribed for appropriate patients. At standard therapeutic doses, short-term treatment is usually without substantial toxicity or development of dependence. At high doses or for prolonged periods of use, toxicity and dependence may increase in frequency and severity. Benzodiazepines are not drugs of abuse, although benzodiazepine abuse is common among people who are actively abusing alcohol, opiates, cocaine, or sedative hypnotics. Clinical evidence suggests that abuse is also more likely among patients with a history of alcoholism. It is important for clinicians to feel comfortable prescribing benzodiazepines for appropriate patients, but the potential for toxicity and dependence must be considered before prescribing. Patients who may receive benzodiazepines for long periods or at high doses should be also informed of these risks.

REFERENCE

1. Benzodiazepine Dependence, Toxicity, and Abuse: A Task Force Report of the American Psychiatric Association. Washington, DC, APA, 1990

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Clarification of Projective Identification

William N. Goldstein, M.D.

This paper clarifies the various current usages of the term "projective identification." The author presents a broad reference model of projective identification based on the work of Ogden. This model divides projective identification into three steps. Step 1 is the projection of a part of oneself onto an external object. Step 1a is the blurring of self and object representations. Step 2 is an interpersonal interaction in which the projector actively pressures the recipient to think, feel, and act in accordance with the projection. Step 3 is the reinternalization of the projection after it has been psychologically processed by the recipient. The different definitions of projective identification are shown to relate to exactly how the term "projection" is conceptualized (in step 1), to whether step 1a is deemed necessary, and to how many of the three steps are required for the definition of projective identification. The author reviews the work of Ogden, Kernberg, Meissner, Sandler, Malin and Grotstein, Porder, and Zinner et al. Six detailed case examples are provided from within and outside psychotherapy to illustrate all three steps of projective identification.

(Am J Psychiatry 1991; 148:153–161)

Dr. A came out of a psychotherapy session feeling inadequate about himself and pessimistic about his work with his patient, Ms. B. He briefly wondered if Ms. B might be better off with a different therapist. Dr. A was quite puzzled about having these feelings and thoughts. He had always believed that he did good work in general and with Ms. B in particular. He took a look at himself and concluded that he was generally an optimistic young man, usually viewing himself as competent and quite adequate. So where did these feelings come from?

It is a rather common occurrence for psychotherapists to leave therapy sessions experiencing some unwanted and uncomfortable feelings. They might, for instance, feel anxious, depressed, overwhelmed, or even confused. Like Dr. A, they might feel inadequate or overly pessimistic. Sometimes they are puzzled by their feelings, being unclear why they feel the way they do. In situations like this, a therapist has learned to look at his or her countertransference—to ask himself or herself, Is there something within myself, based on my past, that has stimulated such a feeling? Am I prone to feeling anxious, am I vulnerable to depression, do I easily feel inadequate? Sometimes the answer does lie in the countertransference, at least partially. Often, however, the answer lies mainly elsewhere.

What is often happening in instances like these is that the therapists have come under the influence of projective identifications. They are feeling uncomfortable not so much because of their own unresolved conflicts (although these should always be considered and never easily discounted) but because the patients have projected these feelings onto them. In fact, not only have the patients projected their feelings onto the therapists, they have done everything in their power to make the therapists accept the projections. They have interacted with the therapists, sometimes overtly, sometimes more subtly, to get them to think, act, and

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The author thanks Virginia Hendrickson, L.C.S.W., for her help with conceptualizing some of the theory and for contributing three of the clinical examples.

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feel in accordance with the projections. Sometimes feeling coerced and pressured, therapists have accepted the projections, frequently not realizing what has taken place. They have responded to the projective identifications, not so much because of their conflicts as related to their countertransference but because of the pressure from the patients for them to receive the projections.

Going back to the example, when Dr. A looked closely at the psychotherapy hour, he could see how Ms. B, suffering from chronic feelings of inadequacy and low self-esteem, had projected these feelings onto him, then acted toward him so that he would accept the projected feelings. Ms. B succeeded in her task, and by the end of the hour Dr. A felt inadequate himself. Ms. B was subtle enough in her interactions with Dr. A so that he was initially puzzled by his feelings.

During the psychotherapy hour, Ms. B first spoke of how worthless she was and how hopeless her condition was. Then she discussed psychotherapy in general, wondering how useful it was in serious cases. She then went on to discuss a series of cases where an inexperienced professional had erred. A young lawyer had made a major mistake that lost him a large amount of money, an inexperienced surgeon had left his patient with an unsightly scar, and a new accountant had totally messed up Ms. B's taxes. Experience was all-important, Ms. B claimed, and asked if Dr. A didn't think so. Ms. B then began to argue her point with Dr. A, insisting that he agree with her. She then recalled a number of stupid blunders Dr. A had made, but said it was "no big deal" because she realized he had just completed his psychiatric training. She viewed her case as a very serious one, yet she knew Dr. A would try as hard as he could. However, she felt she had suffered for so long that possibly no one could help her.

This example shows projective identification in the psychotherapy hour, but this process is not confined to psychotherapy. It is a commonplace phenomenon in day-to-day interactions between friends and acquaintances, as some of the later examples will demonstrate.

As presented in the example of Dr. A and Ms. B, projective identification appears to be a fairly straightforward phenomenon. Yet, because it is currently used in numerous different ways by many different people, it remains a most elusive and difficult concept. It has been described as a primitive defense in patients with borderline and psychotic disorders, a developmental process out of which self and object differentiation comes about, an integral part of the transference-countertransference process in both psychoanalysis and psychotherapy, a form of empathy, and more. Clinically, some view projective identification as a useful and even necessary way of conceptualizing a variety of phenomena, some use the term sparingly but with clear meaning, and others have little use for the concept. For those who use the term, there are many questions. These include the difference between projective identification and projection, the nature of the identification and how it relates to the projection, the role of blurring of ego boundaries in the process, the role of the interaction between the projector and the recipient of the projection, and the nature of the reinternalization process.

Melanie Klein (1) first described projective identification as a process beginning in the earliest time of life, in a phase she called the paranoid-schizoid position. Klein was referring to a process in which parts of the self are split off and projected into another person, leading to a particular kind of identification. This process includes an effort to control the other person by the projected parts. Segal (2) summarized Klein's original description of projective identification in a more succinct manner: "Parts of the self and internal objects are split off and projected into the external object, which then becomes possessed by, controlled and identified with the projected parts" (p. 27). The concept of projective identification has been developed and elaborated by many of Klein's followers, including Bion (3, 4), Rosenfeld (5, 6), and Segal (2). More recent contributions along these lines have been made by Malin and Grotstein (7), Grotstein (8), and Ogden (9–11).

Although always an important concept in the Kleinian school of psychoanalysis, the term "projective identification" attained increasing popularity and became more generally widespread with the publication of Kernberg's work on borderline personality organization (12). Kernberg listed projective identification as one of the borderline defenses, together with splitting, primitive idealization, primitive denial, omnipotence, and devaluation. As will be detailed later in this paper, Kernberg's thinking about projective identification has evolved with time, and his original description of the term is somewhat different from his more recent elaborations (13, 14). The increased use of the term, unfortunately, has not led to a consensus as to its meaning. In fact, there have been new applications of the concept and new ways of looking at projective identification. Examples include the use of the concept by the object-relations-oriented family therapists (15–17) and Porder's innovative and useful thinking about projective identification (18).

The history of the concept of projective identification has been elaborated quite well by others (8, 19, 20) and will not be repeated here. Rather, in this paper I will focus on the various current usages of the term, with the hope of providing added clarification and integration. The emphasis of this paper will be on projective identification as a defense mechanism, especially as it relates to the psychoanalytic and psychotherapeutic processes.

In this paper, explanations of the various aspects and steps of projective identification will be illustrated by clinical examples. Six detailed clinical examples appear at the end of the text, and excerpts from these cases will be interspersed throughout the text at appropriate places. At times it might be useful for the reader to refer to the detailed clinical example after reading an excerpt.

REFERENCE MODEL OF PROJECTIVE IDENTIFICATION

To look at the different current usages of projective identification, I use a broad model of projective identification as a point of reference. This broad model is in accordance with the work of Ogden (9, 10), who originally defined projective identification as a process occurring in three steps. Step 1 involves the fantasy of projecting a part of oneself into another person, with that part controlling the person from within. The projected part is something the individual wishes to be rid of, either because the part threatens to destroy the self from within or because the person feels the part is in danger of attack by other aspects of the self. A distinction is made here between projective identification and projection. In projective identification, the projector feels at one with the recipient of the projection; this feeling of oneness involves a blurring of self and object representations. In contrast, in projection proper, the projector feels estranged from and threatened by the recipient of the projection.

Step 2 is an interpersonal interaction in which the projector actively pressures the recipient to think, feel, and act in accordance with the projection. According to Ogden, projective identification does not exist when there is no interaction of this nature.

Finally, in step 3, the projection is reinternalized after it has been psychologically processed by the recipient. The nature of the reinternalization process depends on the maturational level of the projector and can range from primitive types of introjection to mature forms of identification. Whatever the process, the reinternalization offers the projector the potential for attaining new ways of handling a set of feelings and fantasies that he or she could only wish to be rid of in the past.

More recently, Ogden (11) has clarified that the projection can involve either a self representation or an object representation. He has de-emphasized the concept of controlling the person from within and has backed away from the need for a blurring of self and object representations as necessary to the process. With these recent clarifications, Ogden's concept of projective identification now provides the broadest model today.

Some (13, 21) feel that Ogden's concept of projective identification is too broad. However, it is just that aspect of his work which makes it conducive as a reference to compare the various current usages of projective identification. In using his work as a reference, I will modify and outline Ogden's steps in the following fashion: Step 1 is the projection (or externalization) of part of oneself onto an external object (recipient). Step 1a is the blurring of self and object representations. Step 2 is the interpersonal interaction in which the projector actively pressures the recipient to think, feel, and act in accordance with the projection. Step 3 is the reinternalization of the projection after the projection has been psychologically processed (and modified) by the recipient.

As will be shown in this paper, the different definitions of projective identification relate to exactly how one conceptualizes the term "projection" in step 1, whether step 1a is deemed necessary, and how many of the three steps are required for the process to qualify as projective identification.

Step 1: The Projection

What is meant by the term "projection" is very important because people who use the term "projective identification" differ in their definition of projection. Sandler (22) defines projection as involving a transfer of mental content from a self representation to an object representation. Meissner (21) is basically in agreement with this, stating that projection involves an attribution of part of a self representation to an object representation. Meissner further distinguishes displacement from projection, stating that displacement involves an attribution of part of one object representation to another object representation. Differentiation of projection from displacement in this way is often the norm. Yet Ogden (9, 10) classifies displacement (of one object representation to another) as a form of projection. The question of the definition of projection is crucial here. As will be seen, the process of projective identification takes on different meanings in accordance with what part of the psychic apparatus is projected.

For further clarification, I will first become simplistic and state the obvious, that the psychic apparatus is thought to include the drives (id), the ego, and the superego. Next I will state that I will view self and object representations as parts of the ego (23). Although this is in accordance with the ideas of Sandler and Rosenblatt (24), Jacobson (25), and Kernberg (26), others (27) disagree. Some prefer to think of self and object representations as being formed by the interaction of ego, id, and superego; additionally, some object to combining the representational model with structural theory. However, including self and object representations as parts of the ego allows for an easily understandable model, clearly suitable for the purposes of this paper.

Next, again in accordance with the purposes of this paper, I will simplify things and use the term "projection" in its broadest sense, to include any kind of externalization. Although the term "externalization" is sometimes differentiated from the term "projection," often referring to a larger group of phenomena, it is also widely used as a synonym for projection (22). This latter usage will be applied here. Thus, we can speak of externalizations or projections as referring to drives, self representations, object representations, and superego. Alternatively, one can think totally in accordance with a representational model. Here drives would be conceptualized as self representations (either aggressive self representations or libidinal self representations) and the superego would be conceptualized as an object representation.

Given these simplifications, I will now posit a number of distinctions and ideas regarding step 1 of projective identification. I want to emphasize that these ideas need to be viewed as generalizations only, as ideas that warrant further exploration and thinking.

The nature of projective identification changes in accordance with what is projected. A very important distinction here is between the projection of self representations or drives on the one hand and the projection of object representations or superego on the other. In general, the projection of self representations (or drives) is thought to constitute a more primitive process than the projection of object representations (or superego). Projections of self representations (or drives), when they occur frequently, are most typical of individuals with borderline and psychotic disorders. Regarding the psychotherapeutic process, these types of projections may occur in neurotic individuals, especially in the transference regression in psychoanalysis; however, with the neurotic individual they are neither frequent nor predominant. In contrast, in psychotherapy with patients with borderline and psychotic disorders, these kinds of projections can be both frequent and predominant, even without the use of the couch.

The projection of object representations (or superego) constitutes a different phenomenon. Traditionally, when one thinks of the transference as a repetition of actual relations from the past, fantasized relations from the past, and defenses against both, one is referring to projections of object representations. Projections of object representations (or superego) are ubiquitous; they are commonplace among all individuals, both in day-to-day interactions and within psychotherapy. As noted, projections of object representations are synonymous with displacements. To help illustrate the different types of projection in step 1, I refer now to the clinical examples.

In case 1, Mr. C views his analyst as treating him unfairly and taking advantage of him. This view of his analyst is heightened when Mr. C anticipates that the analyst will charge for a missed session. Mr. C has a long history of feeling taken advantage of and used by his mother. This case is an example of a transference based on the projection of an object representation.

In case 2, Ms. D presents herself as inadequate, little, and pathetic, then feels that her analyst views her in that same way. Actually, her analyst views her as competent and high powered, yet she insists that he sees her as little and inadequate. Here Ms. D is experiencing with her analyst what she continually experienced with her father as a child. This is another, more complicated, example of a transference based on the projection of an object representation. Here Ms. D retains her self representation (little and inadequate) and projects onto the analyst an object representation of someone who treats her in accordance with that self representation.

In case 4, Mr. G views his therapist as worthless and impotent, incapable of doing anything right. In reality the therapist is doing an excellent job. Mr. G, having grown up in an environment where he was continually attacked and belittled by his mother, has internalized an image of himself as worthless and impotent. This case is an example of a transference based on the projection of a self representation of someone worthless and impotent.

In case 5, Mr. H does things to make his girlfriend feel anxious. For example, when in a crisis he leaves out crucial details, which makes the situation seem more dangerous. Then he complains bitterly of his girlfriend's high anxiety. Actually, Mr. H is the one who is overtly anxious, and he deals with his anxiety by projecting it onto his girlfriend. This is an example of the projection of a self representation, of someone who is anxious.

If only projections of self representations (and drives) are included in the definition of projective identification, it refers mostly to a process involving individuals with borderline and psychotic disorders. This process, often thought to include some blurring of ego boundaries, is basically in accordance with the thinking of Kernberg (13, 14) and Meissner (19, 21). If projections of object representations (and superego) are included in the definition of projective identification, and if blurring of ego boundaries is not required, then projective identification refers to a process involving basically all individuals. This is in accordance with the work of Grotstein (8) and with Ogden's more recent use of the term (11). Both Ogden and Grotstein basically view projective identification as a universal feature of the transference. Interesting enough, in the case examples just cited, Mr. C and Ms. D are basically neurotic individuals, whereas Mr. G and Mr. H are psychotic.

At this point, I take the opportunity to relate the considerations just discussed to Meissner's concept of transference (28) and to Racker's concept of countertransference (29, 30). Meissner divides transferences into two groups: projection transferences and displacement transferences. Projection transferences involve projections of self representations, whereas displacement transferences involve projections of object representations. For Meissner, in accordance with what I have already stated, projection transferences are most typical of individuals with borderline and psychotic disorders, whereas displacement transferences are more typical of neurotic individuals. Meissner would view the transferences involving Mr. C and Ms. D, where there are projections of object representations, as displacement transferences. He would view Mr. G as an example of a projection transference. Mr. H would be viewed as a projection transference, but outside of the psychotherapeutic situation.

Meissner's concept of transference corresponds to Racker's concept of countertransference (29, 30). Racker divides countertransference identifications into two types: concordant identifications, where the analyst identifies with the patient's internal structure (or self representations), and complementary identifications, where the analyst identifies with the patient's internal objects (or object representations). The concordant identification corresponds to Meissner's projection transference, and the complementary identification corresponds to Meissner's displacement transference.

Step 1a: The Blurring of Self and Object Representations

It is interesting that both Kernberg (13) and Ogden (9, 10) originally emphasized the blurring of self and object representations as part of projective identification, then moved away from including it in the definition. In more recent descriptions of projective identification by Kernberg (13, 14) and Ogden (11), the blurring of self and object representations has been conspicuously omitted, although neither author states the reasons for the omission.

In his original concept of projective identification, Kernberg (12) stated that it was the lack of ego boundaries per se that led to the identification that followed the projection. The beauty of Kernberg's original concept, in applying it to patients with borderline disorders, is that these patients often exhibit blurring of ego boundaries in close interpersonal relationships, enabling projections in that context to take on the characteristics of projective identification. As stated, in more recent writings Kernberg (13, 14) has removed step 1a from his definition of projective identification. Although in his view projective identification is a more primitive defense than projection itself, it is no longer considered an exclusively psychotic mechanism. However, in Kernberg's view projective identification continues to be typical of individuals with borderline and psychotic disorders and not typical of neurotic individuals.

Like Kernberg, Ogden originally emphasized that in projective identification, "the person involved in such a process is operating at least in part at a developmental level wherein there is profound blurring of boundaries between self and object representations" (9, p. 352). However, in his more recent book (11), Ogden omits this blurring of ego boundaries when he describes projective identification. Certainly, in viewing projective identification as a universal feature of the transference, Ogden no longer thinks in terms of blurring of self and object representations.

In accordance with the discussion of step 1, the blurring of ego boundaries in projective identification might be related to the nature of the projection. Projections of object representations (or superego) basically do not include the blurring of ego boundaries. However, projections of self representations (or drives) frequently include such a blurring. When one thinks about it, the transfer of a self representation to an object representation implies blurring of self and object representations by definition. The question remains as to whether projective identification is basically a psychotic process or not. Kernberg and Ogden were originally of that opinion, and Meissner (21) still is. However, to the extent that the term has been broadened to include projections of object representations (and superego), it has become less exclusively associated with borderline conditions and psychoses.

Illustrations of the blurring of self and object representations occur most clearly in cases 5 and 6, involving a man with borderline disorder and a psychotic man, respectively. In case 5, Mr. H does things to make his girlfriend feel anxious, then complains of her high anxiety level. There is a blurring of an anxious self representation with an anxious object representation. In case 6, Mr. I acts toward his therapist in a very disorganized and disruptive manner. He projects his disorganization onto his therapist but remains totally confused about whether he or she is disorganized. Here there is a blurring of a disorganized self representation with a disorganized object representation.

Step 2: The Interpersonal Interaction

In this step, pressure is exerted by the projector on the recipient of the projection to think, feel, and act in accordance with the projection. Although some limit their concept of projective identification to step 1 and 1a only, most feel that step 2 is crucial in the projective identification process. Ogden states that "projective identification does not exist where there is no interaction between projector and object" (9, p. 359). Step 2 actually expands the concept of projective identification beyond the intrapsychic into the realm of interpersonal. In that regard, Ogden (9, 10) views projective identification as a bridging concept, one that links phenomena in the intrapsychic sphere with those in the interpersonal.

As noted, not everyone is happy with this expansion. In this regard, Meissner (21) differentiates between the one-body context (intrapsychic) and the two-or-more-body context (interpersonal). Meissner regards projective identification as a totally intrapsychic phenomenon and limits his concept to step 1 and 1a. Kernberg (13) minimizes Meissner's differentiation, stating that it is artificial to separate the intrapsychic from the interpersonal. Despite this, Kernberg's original definition of projective identification (12) is basically an intrapsychic one, whereas his more recent definition (13, 14) clearly includes an interpersonal component.

Sandler (20) helps us understand the various usages of projective identification by classifying projective identification into three stages, in accordance with the historical usages of the term. In stage 1, in accordance with Meissner, the processes remain intrapsychic. In stage 2, the analyst becomes involved in the interaction (step 2) by identifying with the projection to a degree sufficient to contribute to the analyst's countertransference. Here, the analyst is influenced by the projection only by his or her identification; the patient does not actively pressure the analyst to receive the projection. It is only in stage 3 that there is a definite interaction, where the analyst is pressured to act in accordance with the projection. In this stage, the opportunity for reinternalization, to be discussed later in this paper, becomes available.

Illustrations of the interpersonal interaction, where pressure is exerted by the projector on the recipient to act in accordance with the projection, appear in all the clinical examples. In case 2, for example, Ms. D presents herself as inadequate, ineffective, little, and pathetic and insists that her analyst view her this same way. She assumes that he agrees with her and presents one example after another based on this assumption. If the analyst states disagreement, she argues vehemently with him. With her persistence, the analyst feels pressured, coerced, overwhelmed, and frustrated.

Case 3 shows the interaction between two physicians during medical rounds. Here Dr. E, who is leading the rounds, projects her own feelings of inadequacy onto Dr. F and then treats Dr. F as if she is, in fact, inadequate, although Dr. F is almost her equal. As a result, Dr. F begins to feel inadequate herself.

In case 5, Mr. H projects his own anxiety onto his girlfriend. He talks to her about crisis situations, making the situations seem much more dangerous than they actually are. He then complains about her high anxiety.

In 1987, Porder (18) presented projective identification in a different and interesting way. His work is mentioned now because it lends more understanding to the interpersonal interaction (step 2). Porder views projective identification as a "two-tiered" transference/countertransference mechanism, understood as a compromise formation that includes as major components identification with the aggressor and/or a turning of passive into active.

To understand Porder's work, I will use his example where, by means of projection in step 1, the analyst is viewed as a powerful aggressive parent, while the patient views himself or herself as a helpless victimized child. In step 2 (the interactive process), the patient becomes active and aggressive in trying to pressure the analyst to accept the projected image of a powerful aggressive parent. As the patient aggressively and forcefully tries to coerce the analyst to accept the projection, the analyst begins to feel helpless and victimized. Through this interpersonal interaction, a role reversal has taken place. The patient has identified with the powerful aggressive parent, turned passive into active, and is now treating the analyst as a helpless victim.

To clarify further, in step 1 the patient projects onto the analyst an object representation of a powerful parent, while identifying with a self representation of a helpless victimized child. Then in step 2, the patient projects onto the analyst a self representation of a victimized child, while identifying with an object representation of a powerful parent. Step 2, in this example, includes a second and different projection and a second and different identification. It should be noted that this is not always the case. For example, if in step 1 a self representation of a little, victimized self is projected, then step 2 simply adds intensity to the original projective process. However, step 2 always involves identification with the aggressor and a turning of passive into active.

Porder states that the interpersonal interactions characteristic of projective identification are more common in individuals with borderline and psychotic disorders. He relates this to the fact that these sicker individuals grow up with more disturbed and aggressive parents (by whom they are victimized and with whom they identify) and to the fact that these individuals have more difficulty expressing their conflicts verbally.

Step 3: The Reinternalization of the Projection

In step 3, the projection is reinternalized after it has been psychologically processed and altered by the recipient. The psychological processing is in accordance with the recipient's psychic structure, including his or her strengths, weaknesses, and defensive system. If the recipient is sufficiently different from the projector, the processed version of the original projection might include substantial changes. According to Ogden (9, 10), the processed version might be modified in such a way that the projector, after the reinternalization, might no longer feel the need to be rid of the now altered projection. Regarding psychotherapy, although the processing of the projection is often thought to take place "silently," interpretations regarding the projection can also be used to influence the reinternalization. The exact nature of the reinternalization process depends on the maturational level of the projector and can vary from primitive types of introjection to more mature forms of identification.

Step 3 extends the concept of projective identification even further. This step has particular relevance to the psychotherapeutic process. The reinternalization process offers the projector the potential for change, for attaining new ways of handling a set of feelings and fantasies that he or she could only wish to be rid of in the past. With that in mind, some (8) have understood the essence of psychotherapeutic change as taking place through a series of projective identifications. The developmental process can be conceptualized in an analogous way.

As might be expected, the expansion of projective identification to step 3 is certainly not uniformly agreed upon. As noted, Meissner (19, 21) confines his definition of projective identification solely to an intrapsychic process, including step 1 and 1a only. Kernberg (13, 14), although he includes step 2 in his definition of projective identification, feels that step 3 would extend the definition too far. Sandler (20) includes the reinternalization process only in what he calls stage 3 of projective identification. Despite these differences, the reinternalization process is now commonly included by many in thinking about projective identification.

Regarding the reinternalization process in psychotherapy, change usually can be noted only after the accumulation of a number of instances of reinternalization of projections. Case 2 demonstrates this. Ms. D presents herself as little and inadequate, repetitively insists that her analyst view her that way, and repetitively argues that, in fact, she is that way. As this process occurs over and over again, the analyst is partially influenced by what Ms. D says (that is, by her projections onto him); yet his basic view of her as competent and high powered remains. With time, Ms. D is able to somewhat alter her self representation because of the reinternalization process. To be more specific, Ms. D repetitively projects onto the analyst an object representation of someone who views her in accordance with her self representation. The analyst is able to receive Ms. D's projections but is minimally influenced by them; he maintains his basic view of her as competent and high powered. One could say that he modifies the projections onto him in accordance with his original view. By accumulative reinternalizations of the modified projections, Ms. D is gradually able to alter her self representation in accordance with the way the analyst views her. Thus, she is gradually able to see herself as less little and pathetic and more competent and high powered.

THE WORK OF ZINNER AND ASSOCIATES

As noted earlier, the concept of projective identification has been expanded to marital and family therapy by a group of object-relations-oriented psychoanalysts. The work of this group—Zinner, R. Shapiro, E. Shapiro, and Berkowitz (15–17)—will be briefly reviewed here and related to the reference model of projective identification.

Regarding marriage, Zinner et al. emphasize mutual projective identifications between the marital couple, where each member willingly (although unconsciously) accepts the projections of the other. For example, a husband maintains a desired image of himself as aggressive and competitive by projecting his unwanted passive and helpless qualities onto his wife. This is ideal for the wife, who is able to maintain her desired image of a passive and helpless woman by projecting her competitive and aggressive qualities onto the husband. Thus, the projective identifications are mutually rewarding and complementary. In the case of parents and their children, projective identifications also can be complementary. More frequently, however, the children, although accepting of the parental projective identifications, suffer considerably as a result of the projections. Still, these children, for a variety of reasons, most important of which might be the fear of object loss, easily accept the parental projections.

In the work of Zinner et al., it is noteworthy that the projections are typically easily accepted. In fact, these authors emphasize the element of (unconscious) collusion. This collusion is in contrast to projective identifications in the psychoanalytic and psychotherapeutic situation. Also of interest is that many of the authors' examples are projections of (unwanted) self representations. Since Zinner et al. appear to work with a wide variety of patients, this could contradict my earlier generalization that the projection of self representations indicates a primitive process. It is quite possible, however, that the projection of a self representation to a clearly accepting recipient involves a less primitive process than the projection of a self representation to a clearly unwilling recipient.

In the work of Zinner et al., there is no requirement of blurring of self and object representations (step 1a), although examples are given where the blurring does occur. The reinternalization process (step 3), especially where there is collusion, is not emphasized. However, in the authors' psychotherapeutic work, reinternalization of the projections plays an important role.

PROJECTIVE IDENTIFICATION VERSUS PROJECTION

A few additional words might be useful to further clarify the distinction between projective identification and projection. As already discussed, many view projective identification as a more primitive process than projection, one that implies at least some blurring of ego boundaries in the area of the projection. It is this blurring of ego boundaries which causes the projector to hold onto, feel at one with, and continue to identify with the projection. In contrast, projection is seen as occurring when there are clearly differentiated ego boundaries. Here the projector feels little identification with the projection and may distance himself or herself and stay away from the object of the projection. This is basically the view of Kernberg (13, 14), certainly that of Meissner (19, 21), and originally that of Ogden (9, 10).

With the broadening of the definition of projective identification (with the inclusion of object representations as well as self representations in step 1, and with the elimination of step 1a as a requirement), the distinction between projective identification and projection is less clear. The extreme here is the elimination of the distinction, as in the idea of Malin and Grotstein (7) that the projector always retains some contact (and identification) with what is projected. In essence, the distinction between projective identification and projection varies in accordance with the definition of projective identification.

CLINICAL EXAMPLES

Some of the following cases are from psychoanalyses, others from psychotherapy, and still others from interactions outside of psychotherapy. Individuals with neurotic, borderline, and psychotic disorders are all included. The examples show projections of both self representations and object representations. In several cases there is blurring of ego boundaries. All cases include the interpersonal interaction, where the defenses of identification with the aggressor and the turning of passive into active can be noted. Excerpts from these cases have already been referred to throughout this paper.

Case 1. Mr. C grew up with a mother who seldom listened to him, who constantly forced her will on him, and who never gave him any choices or alternatives. In regard to this, Mr. C felt treated unfairly, taken advantage of, and used. As might be expected, he usually viewed his psychoanalyst analogously to his mother. In fact, Mr. C went out of his way to create situations so that he could think of the analyst that way. Additionally, he induced his analyst to act in accordance with his thinking, then raged at him for his unfair treatment. For example, after clearly agreeing to a policy of paying for missed sessions unless the analyst filled the hour, Mr. C felt that he should not have to pay for an appointment at the time of a rescheduled graduate class. Mr. C assumed that the analyst would charge if he missed and felt taken advantage of and cheated. He repetitively chastised and criticized the analyst about how unfair he was, insisting that the analyst had forced his will on him and would not listen to his point of view. The analyst began to feel both guilty and angry; he felt that maybe he was being unfair to Mr. C and taking advantage of him. He also felt harassed, forced to take the position ascribed to him, and treated poorly by Mr. C. Later it turned out that Mr. C had several other time options regarding the rescheduled class but had neglected to mention that.

In this example, Mr. C projects a maternal object representation onto the analyst, creates situations where he can view the analyst in accordance with this projection, and then tries to force the analyst into accepting the projection.

Case 2. Ms. D, although she functioned in a highly competent fashion and was widely respected in her profession, frequently presented herself in psychoanalysis as inadequate, ineffective, little, and pathetic. She said she was a loser, was inferior to her colleagues, and was looked down upon and scorned by her fellow professionals. Ms. D insisted that her analyst view her in the same way that she saw herself and repetitively acted to get him to feel and to treat her that way. In a manner particularly annoying to the analyst, Ms. D acted as if it were a fact that the analyst agreed that she was little and inadequate. She elaborated one example after another, based on the assumption that the analyst agreed with her. If the analyst made any comment indicating that he felt differently, Ms. D would argue with him and insist that he was being stupid and demeaning. The analyst felt pressured, coerced, overwhelmed, frustrated, and angry.

Here Ms. D retains her self representation as a little, pathetic, devalued professional while projecting onto the analyst an object representation of a demeaning, devaluing, and critical parent. Note that the self representation is retained; it is the object representation (of someone who treats Ms. D in accordance with her self representation) that is projected. Ms. D here interacts very provocatively with the analyst as she tries to get him to accept her projection.

Case 3. As a defense against her own feelings of inadequacy, Dr. E referred to herself in a very exaggerated fashion as an important and knowledgeable member of the senior staff. In charge of making medical rounds, she treated a colleague, Dr. F, as if Dr. F were inadequate. Although Dr. F was almost her equal, Dr. E lectured her and quizzed her as if she were a beginning medical student. When Dr. F did not know something, Dr. E would sigh in disbelief. As this sequence of events continued, Dr. F, also somewhat lacking in self-confidence, began to feel inadequate herself.

This is an example of projective identification outside the psychotherapy setting. Here Dr. E projects a self representation onto Dr. F and then treats Dr. F in accordance with this projection, doing everything possible to make Dr. F accept the unwanted projected feelings.

Case 4. Mr. G, a man with schizophrenia, verbally attacked his therapist. Session after session he yelled and screamed that the therapist was not helping him, that she was worthless and impotent, and that she was incapable of doing anything right. Whatever the therapist did or said, Mr. G immediately jumped on it as wrong and indicative of her inability to help. As the attacks continued, the therapist began to feel worthless, impotent, and destroyed. Exploration revealed the interaction to be a reenactment with a role reversal of Mr. G's relationship with his mother, in which he felt worthless and destroyed by her continual verbal attacks on him.

In this case, Mr. G projects a self representation onto his therapist, then repetitively treats the therapist in accordance with the projection. The therapist begins to view herself in accordance with the projection.

Case 5. Mr. H, a man with a diagnosis of borderline personality disorder, was in a relationship with a highly anxious woman. This man lived from crisis to crisis, yet gave the appearance of utmost calm, that he could deal with anything. He complained bitterly of his girlfriend's high anxiety, yet in telling her about his situations he would inevitably leave out crucial details, making the situation seem much more dangerous than it actually was. Mr. H would thereby increase his girlfriend's anxiety and then attempt to distance himself from her to get away from the anxiety. Paradoxically, he could not tolerate even a day without contact with her because absence of contact increased his anxiety.

Here is another example of projective identification outside of the psychotherapy session. Here Mr. H rids himself of his anxiety by projecting his self representation onto his girlfriend. In a subtle but clear manner, he relates to his girlfriend in a way that induces her to feel and act in accordance with the projection. In this case, the blurring of self and object representations is noted by Mr. H's unclarity about who is anxious, himself or his girlfriend. There is a blurring of an anxious self representation with an anxious object representation. This blurring is also evident in Mr. H's inability to make this projection totally, as shown by his need for daily contact with his girlfriend.

Case 6. Mr. I, a man with a diagnosis of paranoid schizophrenia, had difficulty writing his check at the end of one session. He could not spell words; he could not remember the date or to whom to write the check. Obviously in a disorganized state, he said to the therapist that he was dangerous and bad and that she had better watch out or he would mess up her thought processes. He then started acting in a very disorganized and disruptive manner. He told the therapist that she was rigid and inflexible as he was going over his hour; then he reversed himself and said no, it was he who was rigid and inflexible. He called the therapist bad names; then he said maybe it was he rather than she who was bad. He said he did not ever want to see the therapist again, yet had a hard time leaving. When he left, the therapist felt very unsettled and disorganized herself.

This is a case where a disorganized self representation is projected onto the therapist. By being exposed to the ramifications of Mr. I's disorganization, the therapist is left feeling that same way herself. In this case, the blurring of self and object representations is most clear: Mr. I has difficulty distinguishing himself from the therapist.

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Insights Into the Structure and Function of GABA-Benzodiazepine Receptors: Ion Channels and Psychiatry

Charles F. Zorumski, M.D., and Keith E. Isenberg, M.D.

Objective: As a result of combined biophysical and molecular biological studies, important insights into the structure and function of γ-aminobutyric acid (GABA) receptors have been achieved. These insights have helped to define the role of GABA receptors in synaptic inhibition and the ion channel mechanisms by which different neuropsychiatric drugs work. The authors' goal is to describe the actions of GABA as a neurotransmitter and discuss the modulation of receptor function by different drugs. Data collection: The authors focus on more recent studies of the structure and physiology of the receptor-ion channel complex and the relevance of these studies to psychiatry. Findings: The CNS effects of benzodiazepines, barbiturates, and alcohol have been linked to the GABA-chloride channel receptor complex. Multiple subunits of this complex have been cloned, sequenced, and expressed in heterologous systems. The results of cloning studies, coupled with membrane biophysics, have provided important insights into the structure and function of GABA receptors and their modulation by psychopharmacological agents. Conclusions: Future understanding of disease states, drug effects, and therapeutic successes and failures may be expressed in terms of differences in the structure and function of specific receptors and their associated ion channels. Furthermore, the ability to describe the molecular function of receptor subtypes offers the ability to tailor drug specificity by developing agents directed against a given receptor subtype. The current GABA studies also have important implications for the understanding of how neurotransmitter systems may be involved in illness.

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An implicit goal of biological psychiatry is to understand the neural mechanisms involved in specific clinical syndromes. One means of gaining this understanding is through investigations into the mechanisms of psychotropic drug action. The effects of different drugs on the γ-aminobutyric acid (GABA) neurotransmitter system suggest that this system is involved in several forms of neuropsychiatric pathology. Perhaps the strongest evidence linking GABA to an illness is found in epilepsy, where pharmacological, biochemical, and anatomical data support the involvement of the transmitter. Drugs that enhance GABA actions, which include the barbiturates and benzodiazepines, have proven efficacy as anticonvulsants (1). In contrast, agents that inhibit GABA responses, including bicuculline, picrotoxin, and pentylenetetrazole, have prominent convulsant effects (2). Animal studies also suggest that in epileptic foci there is altered functioning of GABAergic interneurons (3), which leads to a loss of local inhibition and hyperexcitable collections of neurons driving electrical seizure discharges.

The evidence linking GABA to specific psychiatric disorders is less direct, but it appears that the GABA receptor complex is a major site of action of several psychoactive agents. Hypotheses based on the known pharmacology of benzodiazepines and barbiturates (4) have been generated regarding the role of the GABA system in anxiety disorders (5–9) and sedative-hypnotic abuse syndromes (10). Additionally, data suggest that alcohol exerts certain CNS effects through the GABA complex (11–13). These observations, coupled with the known cross-tolerance between alcohol and

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sedative-hypnotics, have prompted theories regarding a role for GABA receptors in the neurobiology of alcoholism (14).

In addition to these disorders, there is evidence, albeit at times indirect and circumstantial, linking the GABA system to Huntington's chorea (15), tardive dyskinesia (16), depression (17), and schizophrenia (18). Although it is unlikely that GABA is the site of a primary defect in all of these disorders, molecular biological studies have revealed a surprising level of receptor complexity compatible with a role for this transmitter system in more than one disorder. As a result of combined biophysical and molecular biological studies, important insights into the structure and function of GABA receptors have been achieved. These insights have helped to define the role of GABA receptors in synaptic inhibition and the ion channel mechanisms by which different neuropsychiatric drugs work. In this paper, we will describe the actions of GABA as a neurotransmitter and discuss the modulation of receptor function by different drugs. We will emphasize more recent studies of the structure and physiology of the receptor-ion channel complex and the relevance of these studies to psychiatry.

GABA AS A NEUROTRANSMITTER

GABA is thought to be the major inhibitory transmitter in the vertebrate CNS, being used by as many as 40% of neurons (1). GABA is synthesized from L-glutamate by the enzyme glutamic acid decarboxylase (19). Glutamic acid decarboxylase has proven to be an important enzyme in studying the GABA system because it is present only in neurons using GABA as a transmitter. The enzyme has been purified to homogeneity and its regulation studied in detail. Studies using antibodies directed against glutamic acid decarboxylase have revealed that GABA is primarily a transmitter of local inhibitory circuits throughout the CNS (20). This localization differs from catecholamines and serotonin, which are synthesized in discrete, diffusely projecting nuclei in the brainstem and midbrain (21). The local circuit actions of GABA put this transmitter in a unique position to alter rapidly the excitability of primary output neurons. In this way GABA is able to regulate the background tone of neural responsivity. In addition to its use in local circuits, there are two longer tracts that use GABA as a transmitter: the path from the striatum to the lateral globus pallidus and the tract from the cerebellar inferior olivary nucleus to the vestibular nucleus.

In addition to being synthesized by neurons, GABA satisfies several other neurotransmitter criteria. The agent is released from neurons in a calcium-dependent fashion and interacts with specific classes of receptors to generate physiological responses. Exogenous applications of GABA to neurons bearing these receptors mimic the actions of the native transmitter. Similarly, GABA antagonists block the actions of both exogenously applied GABA and the native transmitter. The effects of GABA are terminated by high-affinity sodium-dependent uptake systems in nerve terminals and glia. In nerve terminals, GABA is catabolized to succinic acid semialdehyde by the enzyme GABA transaminase. GABA transaminase, like the GABA synthetic enzyme glutamic acid decarboxylase, has been purified to homogeneity and its distribution in the CNS studied. However, unlike glutamic acid decarboxylase, GABA transaminase is not localized to GABA-containing neurons and appears to serve the more general purpose of removing excess GABA in various regions (21).

GABA RECEPTORS

GABA exerts its physiological actions at two classes of receptors, designated $GABA_A$ and $GABA_B$ (22). These receptors can be distinguished pharmacologically and physiologically. $GABA_B$ receptors represent the minority of GABA sites in the vertebrate CNS and are activated by GABA and by the antispasticity agent baclofen but are insensitive to benzodiazepines or barbiturates. Since $GABA_A$ receptors are thought to be a major site of action for sedatives and anxiolytic agents, we will focus on the properties of this class of receptors and not consider $GABA_B$ receptors further.

At type A receptors, GABA promotes the direct opening of chloride-selective ion channels (23). In most neurons, electrochemical gradients drive the influx of chloride into neurons, thus hyperpolarizing the membrane and inhibiting cell firing. $GABA_A$ receptors are activated by GABA and the hallucinogen muscimol (24). These receptors are inhibited competitively by bicuculline and noncompetitively by a variety of agents, including picrotoxin, t-butylbicyclophosphorothionate, penicillin, pentylenetetrazole, and others (25). Interestingly, agents that inhibit $GABA_A$ function act as convulsants, presumably by mediating a decrement in $GABA_A$-mediated inhibition.

In addition to having sites for agonists and the inhibitors already mentioned, the $GABA_A$ complex is also a site of action for potentiating compounds such as barbiturates, benzodiazepines, steroid anesthetics, and ethanol. These agents, acting by several distinct mechanisms, augment chloride currents that flow through the $GABA_A$ ion channel (4). Evidence now suggests that the $GABA_A$ complex may be a primary site of the sedative-anxiolytic effects of these agents in the CNS. Table 1 presents an overview of the physiological pharmacology of $GABA_A$ receptors.

GABA activates chloride currents in a dose-dependent fashion. In most systems, the dose-response data yield a Hill coefficient of 2, which implies that opening of the chloride channels requires the cooperative interaction of two molecules of agonist (26). GABA typically activates physiological responses over low micromolar concentrations with maximal responses near 100 μM (27). In addition to this dose-dependent acti-

TABLE 1. Ion Channel Pharmacology of GABA$_A$ Receptors

Drug	Site of Action	Mechanism	Clinical Effect
Agonists			
GABA	GABA binding site	Opens chloride selective ion channels	Inhibitory neurotransmitter
Muscimol	GABA binding site	Opens chloride channels; other mechanisms possible	Hallucinogen
Inhibitors			
Bicuculline	GABA binding site	Competitive inhibition; decreases affinity of GABA	Convulsant
Picrotoxin	t-Butylbicyclophosphorothionate binding site	Noncompetitive inhibition; no effect on GABA affinity; decreases flow of chloride ions	Convulsant
Diazepam-binding inhibitor	Benzodiazepine binding site	Noncompetitive inhibitor; exact mechanism unknown; benzodiazepine inverse agonist	Convulsant; anxiogenic; endogenous agent
β-Substituted γ-butyrolactones	γ-Butyrolactone binding site, possibly	Mixed inhibitor	Convulsant
Zinc or calcium ions	Not known	Decreases affinity of GABA; calcium works intracellularly	Increases neural excitability, possibly
Phenothiazines	Not known	Noncompetitive inhibition; increases GABA desensitization	Convulsant, possibly
Tricyclic antidepressants	t-Butylbicyclophosphorothionate binding site, possibly	Noncompetitive inhibition	Convulsant, possibly
Potentiators			
Barbiturates	t-Butylbicyclophosphorothionate binding site, possibly	Prolongs chloride channel lifetime	Anticonvulsant; sedative; anxiolytic
Benzodiazepines	Benzodiazepine binding site	Increases affinity of GABA; no effect on channel properties	Anticonvulsant; sedative; anxiolytic
Alcohol	Benzodiazepine binding site, possibly	Increases flow of chloride ions; mechanism not known	Sedation
α-Substituted γ-butyrolactones	γ-Butyrolactone binding site, possibly	Increases frequency of chloride channel openings	Anticonvulsant

vation, GABA$_A$ responses exhibit concentration-dependent desensitization. That is, in the presence of continued GABA administration, chloride currents are not maintained but gradually decrease. This fade in response occurs slowly over the course of seconds. The physiological importance of desensitization is uncertain, but the process may serve as a means of limiting GABA-mediated inhibition during periods of excessive transmitter release (28).

A combination of biochemical and electrophysiological studies has allowed detailed examination of the mechanisms of different drugs affecting GABA$_A$ responses. There are two broad classes of GABA-inhibiting agents: the competitive antagonists, which act at the GABA binding site, and the noncompetitive antagonists, which act at sites in the GABA-gated chloride channel. Bicuculline, an example of a competitive antagonist, competes with GABA for binding at the agonist recognition site but does not produce a physiological response. As a result, bicuculline decreases the apparent affinity of GABA for the receptor but does not alter the maximal GABA response (29). Thus, if increasing concentrations of GABA are applied with a fixed concentration of bicuculline, the inhibition can be overcome. In contrast, noncompetitive antagonists such as picrotoxin and t-butylbicyclophosphorothionate do not interfere with GABA binding; i.e., they do not alter the affinity of GABA for its recognition site but, rather, act at a separate locus to impede the flow of chloride ions through the channel. Picrotoxin, for example, decreases maximal GABA responses, a decrement that cannot be overcome by increasing concentrations of agonist (30). The exact ion channel mechanisms by which picrotoxin exerts its effects are unclear because the agent does not appear to be a simple open channel blocker but, rather, may exert complex allosteric effects on the channel conformation (31). The actions of picrotoxin also exhibit use dependence, suggesting that the ion channel must open to allow the inhibitor access to its site of action.

Both competitive and noncompetitive GABA antagonists produce clinical convulsions. This observation has prompted hypotheses regarding the convulsant propensities of other medications and the prediction that drugs which inhibit GABA-gated chloride currents will exhibit epileptogenic properties (2). To the limited extent that this hypothesis has been tested, the prediction that GABA inhibitors act as convulsants has held up. Interestingly, both the tricyclic antidepressants (32, 33) and the phenothiazines (34) exhibit dose-dependent GABA-inhibiting effects that may contribute to their convulsant side effect profiles. The mechanisms underlying the actions of the phenothiazines have been studied at the level of single ion channels. These agents are noncompetitive GABA antagonists and act by a complex mechanism that includes augmenting the rate of desensitization without affecting the open time of the chloride channel (35). Not all antipsychotics share

TABLE 2. Interactions of Drugs With the GABA-Benzodiazepine Receptor Complex

Class of Agent	Example	Mechanism
Agonist	Diazepam	Augments GABA-mediated inhibition
Antagonist	RO15-1788	Blocks benzodiazepine agonists; no direct effect on GABA responses
Inverse agonist	Diazepam-binding inhibitor	Diminishes GABA-mediated inhibition

this GABA-inhibiting property. For example, haloperidol has no effect on GABA currents at concentrations up to 100 μM (34). In contrast, trifluoperazine is a relatively potent GABA-inhibitor, exerting effects at high nanomolar concentrations. The exact site of action for these effects is uncertain, but binding studies suggest that the antidepressants interact with the t-butylbicyclophosphorothionate/picrotoxin site (33). Although the mechanism responsible for seizure generation remains uncertain and is likely to involve complex interactions among neurotransmitter systems, the effects of antipsychotics and antidepressants on $GABA_A$ ion channels warrant further investigation.

Several classes of psychotropic medications are positive modulators of $GABA_A$ responses. Both barbiturates and benzodiazepines interact with the GABA complex to augment chloride currents. Barbiturates, by binding to sites distinct from the GABA recognition site, increase the affinity of GABA for its receptor and, in some preparations, augment chloride currents produced by saturating concentrations of GABA (36, 37). Barbiturates increase GABA responses by prolonging the length of time that chloride channels remain open. After treatment with barbiturates, the mean channel open time increases 4–5 times, without change in the single channel current amplitude. As a result, chloride flows through the GABA channel for a substantially longer time after the channel is exposed to barbiturates (4, 31, 38). Additionally, some barbiturates, particularly those used in anesthesia such as pentobarbital, actually open chloride channels in the absence of GABA (39). The exact site at which barbiturates exert their action remains controversial, but there is evidence that the receptor may be identical to or near the picrotoxin binding site (25). It has been observed that steroid hormone metabolites and anesthetic steroids such as alphaxalone have a mechanism of action similar to that of the barbiturates (40). The steroid hormones may represent endogenous modulators of $GABA_A$ inhibition.

Benzodiazepines act on the $GABA_A$ receptor at sites distinct from those of barbiturates and GABA to alter GABA-mediated responses. It has become apparent that benzodiazepine receptors exhibit complex pharmacology (6, 7): these sites bind molecules that augment, inhibit, or have no effect on GABA responses (see table 2). Current evidence suggests that benzodiazepines act at two different receptor types, termed type I and II, in the vertebrate CNS. Several agents, including CL 218872, quazepam, and zolpidem, have been used to distinguish these sites on the basis of binding affinities. Type I receptors, which have a higher affinity for CL 218872, represent the predominant benzodiazepine receptor in the CNS, but type II receptors are concentrated in the hippocampus, striatum, superior colliculus, and neocortex (41). Interestingly, CL 218872 exhibits effects in animals compatible with an anxiolytic action but is much less sedating than nonselective benzodiazepines such as diazepam (42). These results suggest that different benzodiazepine receptors, coupled to $GABA_A$ receptors, may be responsible for anxiolytic and sedative effects, raising the possibility that more selective psychotherapeutic agents can be developed.

A benzodiazepine binding site pharmacologically distinct from that associated with the $GABA_A$ receptor has also been described (43). This protein is found in the brain and peripheral tissues and is associated with mitochondria. The function of these peripheral-type receptors is unclear because a potent agonist for these sites (RO5-4864) is devoid of anxiolytic effects, despite clearly interacting with receptors in the CNS (44). However, insults to the brain, tumors, and chronic ethanol treatment increase the density of these sites (45, 46), suggesting that peripheral-type receptors may play a role in adaptive metabolic responses (43). Additionally, diazepam exhibits substantial affinity for peripheral-type receptors in the brain, raising the possibility that these receptors may account for some CNS effects of the drug (42).

The complex interactions of benzodiazepines with the $GABA_A$ receptor have led to the concepts of receptor agonists, antagonists, and inverse agonists (6, 7, 47). Benzodiazepine agonists include the commonly used anxiolytics such as diazepam and chlordiazepoxide. These drugs augment GABA-mediated inhibition by increasing the affinity of GABA for its receptor. Benzodiazepines do not directly alter the properties of the chloride channel but, rather, enhance the ability of GABA to open the channel (4). As a result, the degree of effect of a benzodiazepine on a GABA response depends on the concentration of GABA. At low GABA concentrations, benzodiazepines produce a marked effect. At saturating agonist concentrations, benzodiazepines have no enhancing effect (48). This interesting property imparts a possible regional selectivity to the action of benzodiazepines. Whether benzodiazepines alter GABA-mediated synaptic inhibition depends on the native affinity of the receptor for GABA and on the amount of transmitter released at a synapse. Highly efficient synapses that may work at near saturation will be little affected, whereas other synapses exposed to lower GABA concentrations will be greatly enhanced. The lack of effect on maximal GABA responses may, in part, account for the lower toxicity of benzodiazepines compared with barbiturates in overdose cases.

The GABA-enhancing effects of benzodiazepine agonists can be blocked by antagonists such as RO15-1788

(49). These antagonists do not alter GABA responses themselves but block the actions of benzodiazepine agonists and inverse agonists. The inverse agonists have the opposite effect of agonists, decreasing GABA-mediated chloride responses. Diazepam-binding inhibitor may be an example of an endogenous benzodiazepine inverse agonist because this 104-amino-acid peptide interacts with benzodiazepine sites and blocks GABA-gated responses (22, 50). Diazepam-binding inhibitor has anxiogenic properties in vivo, an observation consistent with a role as an inverse agonist. To date, endogenous agonists for benzodiazepine receptors have not been identified (51).

Benzodiazepine agonists have proven useful as sedatives and in the treatment of anticipatory and generalized anxiety. The benzodiazepine antagonists and inverse agonists are being examined for potential clinical utility as antidotes in intoxication syndromes and as cognitive enhancers, respectively. Interestingly, studies using benzodiazepine antagonists have suggested that the benzodiazepine receptor may be a primary site for the sedative and intoxicating actions of alcohol. Alcohol augments GABA-mediated chloride responses (11, 12), and the benzodiazepine antagonists RO15-4513 and RO19-4603 reverse signs of alcohol intoxication in animals (52, 53). The interaction between ethanol and benzodiazepine binding site ligands is complex (54), and this complexity may reflect the multiplicity of $GABA_A$ receptor subtypes.

To complicate further the pharmacology of the GABA-receptor complex, the existence of additional regulatory sites has been suggested. The substituted γ-butyrolactones are convulsant and anticonvulsant molecules that alter GABA currents by binding to a site which appears to be different from the benzodiazepine or barbiturate sites (55–57). Additionally, the GABA complex can be regulated by physiological concentrations of divalent cations such as zinc and calcium (58, 59). The exact mode of action of these divalent cations is uncertain, but both diminish the affinity of GABA for its receptor (29, 58). The actions of calcium are exerted through an intracellular locus (59), suggesting a means by which $GABA_A$ inhibition can be modulated endogenously.

STRUCTURE OF $GABA_A$ RECEPTORS: BIOPHYSICAL STUDIES

Given the complex pharmacology of GABA receptors, a major question concerns how drugs interact with the receptor structure to alter its function. Within the past several years, considerable effort has been expended in understanding these issues and, as a result of a combination of membrane biophysics and molecular biology, a detailed view of the receptor achieved.

In an elegant series of studies conducted in cultured spinal cord neurons, Hamill et al. (23) and Bormann et al. (60) used voltage-clamp and single-channel recording techniques to define the electrical characteristics of the GABA-chloride channel. To examine the relative permeabilities of anions and estimate the size of the channel pore, these investigators substituted other anions for chloride; these anions ranged in hydrated size from thiocyanate (smallest) to isethionate (largest). On the basis of their observations, the GABA channel is estimated to be about 6 Å in diameter. This observation has important consequences for the structure of the protein constituting the channel. If GABA receptors, like other membrane-spanning proteins, are composed of α-helices, each with an average diameter of about 8.4Å, a pore size of 6Å predicts that the channel is formed by five α-helices.

Bormann et al. (60) were also concerned with how GABA channels establish selectivity for chloride over other ions present in physiological solutions. A pore of 6Å is too large to select among chloride, sodium, potassium, and calcium on the basis of ion size alone. Using studies of relative permeability and conductance (a measure of the ease with which ions traverse a channel), Bormann et al. (60) determined that anions must interact with the channel walls in at least two sites to establish the selectivity observed. By binding to sites within the channel, chloride ions line the channel and occlude the flow of other ions through the channel. These observations predict that within the GABA channel there are at least two sites where positive charges are clustered. It is at these sites of positive charge that anions interact to establish selectivity. These sites are also where drugs are likely to interact with the complex.

STRUCTURE OF $GABA_A$ RECEPTORS: MOLECULAR BIOLOGY

Biophysical studies (60) place two constraints on the structure of $GABA_A$ channels: 1) the channels are formed by a pentameric protein and 2) the channels are not simply water-filled pores but, rather, contain binding sites for anions traversing the channel. Within the past 3 years the cloning and sequencing of $GABA_A$ receptor subunits have allowed these predictions to be examined at the structural level.

Early biochemical studies demonstrated purification of the $GABA_A$ complex by using solubilization in zwitterionic detergents and retrieval on benzodiazepine affinity columns (61). The purified receptors retained many of the characteristics of native $GABA_A$ receptors, including high-affinity binding sites for GABA/muscimol, benzodiazepines, and picrotoxin/t-butylbicyclophosphorothionate (62). The maintenance of the picrotoxin site required the presence of phospholipid in the detergent solution, suggesting that it may be associated with membrane lipid (61, 63). The $GABA_A$ receptor was found to be an acidic glycoprotein with a minimum size of 240–290 kilodaltons (kD), consisting of at least two subunits, α and β, of 50–60 kD each.

The results of these protein chemistry studies suggest a mature receptor of no fewer than four and no more than six subunits. Photoaffinity labeling using flunitrazepam for benzodiazepine sites and muscimol for the GABA binding sites (64–66) suggested that the benzodiazepine receptor was associated with the α-subunit (63) and that the GABA site was associated with the β-subunit.

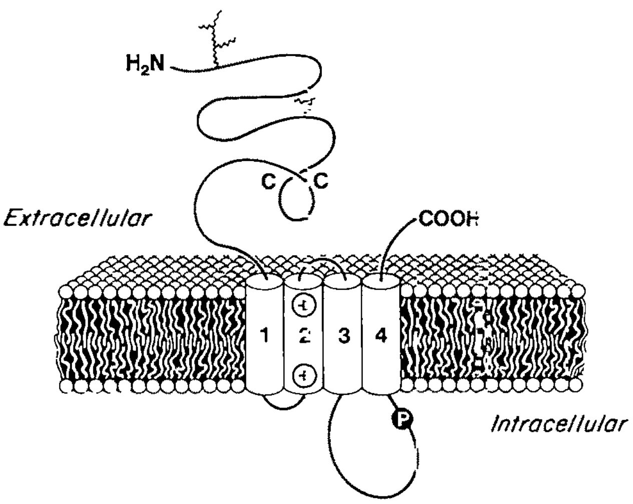
A major advance in the biochemical understanding of the $GABA_A$ complex came when a group of investigators headed by Eric Barnard and Peter Seeburg used receptor purified from bovine cerebral cortex to obtain partial amino acid sequences (67). These investigators constructed short synthetic DNA probes on the basis of the amino acid sequence. These probes were used to screen bovine and calf complementary DNA libraries and isolate clones containing the entire receptor coding region. From these complementary DNAs, the complete primary amino acid sequences of the $GABA_A$ α- and β-subunits were deduced. Analysis of the deduced amino acid sequences indicated that both subunits have four putative membrane-spanning regions of 20–30 hydrophobic amino acids. Each subunit is thought to traverse the membrane four times; the hydrophobic regions are positioned in the lipid bilayer of the cell membrane. This predicted structural feature is shared with nicotinic acetylcholine and glycine receptor subunits but differs from G-protein coupled receptors, which have seven transmembrane-spanning regions (68, 69).

$GABA_A$ receptors share other structural features with nicotinic receptors. Overall there is 15%–20% sequence similarity between the GABA subunits and nicotinic receptor subunits. The first transmembrane-spanning region of $GABA_A$ receptor subunits shows 34% similarity in amino acid sequence with nicotinic receptor subunits, strongly suggestive of subunit homology. $GABA_A$ and nicotinic receptors are predicted to have an extracellular protein loop formed by disulfide bonds between precisely conserved cysteine molecules (positions 139 and 153 of the GABA receptor α-subunit). This loop may be important for the binding of various drugs to the complex and for imparting the change in receptor structure that allows chloride channels to open and close. Both GABA and nicotinic receptor subunits are glycoproteins with sites for the addition of extracellular sugar residues. The β-subunit also contains a consensus site for intracellular phosphorylation by cAMP-dependent protein kinase. Both the amino and carboxy ends of the $GABA_A$ receptor are predicted to be extracellular (70). The structural similarities of $GABA_A$, nicotinic, and glycine receptors have led to the hypothesis that they constitute a gene "superfamily" of ligand-gated receptors which evolved from a common ancestral predecessor. A model for the $GABA_A$ receptor subunits is shown in figure 1.

The biochemical features of $GABA_A$ subunits just described are interesting but do not demonstrate that the subunits form a functioning receptor protein. This proof came from experiments using α- and β-subunit mRNAs expressed in Xenopus oocytes. These frog eggs do not normally express receptors for most transmitters, but when injected with appropriate mRNA they have the machinery to produce functioning receptor-channel proteins. Initial experiments with injection of α- and β-subunit mRNAs into Xenopus oocytes demonstrated that the subunits form a receptor-channel complex which is activated by GABA and is selectively permeable to chloride ions (67, 71). Currents gated by these expressed receptors were augmented by barbiturates and inhibited by bicuculline and picrotoxin. Reconstitution of benzodiazepine responses proved more elusive because simple expression of α- and β-subunits alone or in combination gave inconsistent results (67, 71–73).

Recently, the existence of additional $GABA_A$ subunits has been reported (74). One subunit, designated γ2, appears to be critical for the expression of benzodiazepine sensitivity. Reliable benzodiazepine binding and physiological responses are obtained only when this subunit is coexpressed with α- and β-subunits (75). From these experiments it appears likely that the functioning GABA-benzodiazepine receptor complex is composed of α-, β-, and γ-subunits in an as yet undetermined stoichiometry. It is currently unclear whether the benzodiazepine binding site is restricted to the γ2-subunit, but initial biochemical studies report-

FIGURE 1. Model for the $GABA_A$ Receptor Subunits[a]



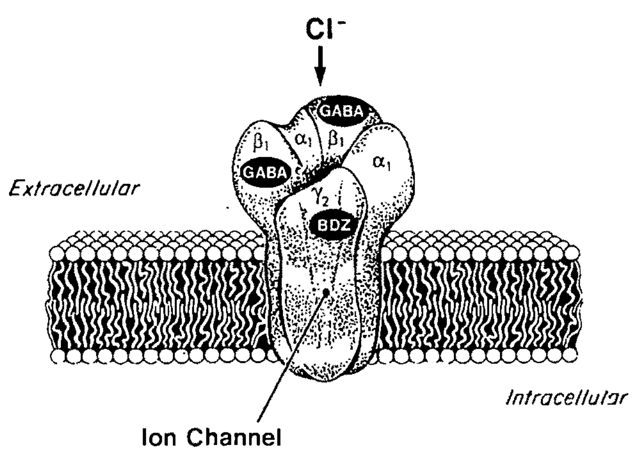
[a] This diagram of a $GABA_A$ receptor subunit shows four membrane-spanning regions. The figure depicts the amino acid backbone of a receptor subunit (dark line) with both the amino (H_2N) and carboxy (COOH) termini in the extracellular space. On the amino terminal portion of the molecule are sights for glycosylation (branches). A disulfide bridge between paired cysteine (C) residues produces an extracellular loop in the molecule. The hydrophobic regions of the protein span the membrane four times (cylinders). At the extracellular and intracellular sides of the protein are collections of positively charged amino acids (+), which provide sites for interaction with chloride ions as they traverse the channel. On the intracellular loop between the third and fourth transmembrane-spanning regions of the β- and γ2-subunits is a consensus site for phosphorylation (P) by cAMP-dependent protein kinase.

ing photoaffinity-labeled benzodiazepine binding to α-subunits would have overlooked the γ2-subunit.

Other cloning experiments have revealed the existence of multiple subtypes of the α-, β-, and γ-subunits and the existence of other structurally related subunits (76, 77). Present evidence indicates that there are at least six different α-subunits (α1–α6), three β-subunits (β1–β3), two γ-subunits, a δ-subunit, and an ε-subunit expressed in the vertebrate nervous system (78, 79). The different α-subunits alter receptor affinity for GABA when expressed with the β1-subunit. α1 yields a high-affinity receptor and is the most abundant GABA receptor α-subunit mRNA in neocortex, hippocampus, and cerebellum. α2 produces a lower-affinity receptor that is the least common α-subunit mRNA in these areas. The α3-subunit results in the lowest receptor affinity for GABA. Expression of α3 appears to be developmentally regulated: mRNA expression is prominent 12 days postnatally in cerebellum but declines subsequently (80). Of considerable interest for psychiatry is the observation that heterogeneity among α-subunits may determine the diversity of benzodiazepine pharmacology in different regions of the nervous system (81). The α3-subunit, when expressed with β1- and γ2-subunits, gives a much greater potentiation of GABA responses by benzodiazepines than either the α2- or α3-subunits. Expression of α2- and α3-subunits with β1- and γ2-subunits produces receptors with pharmacological profiles similar to type II benzodiazepine receptors, and α1-containing receptors exhibit type I pharmacology (81). Recent data using expression of α5-, β3-, and γ2-subunits suggest that benzodiazepine pharmacology may be even more complex (82). This receptor has binding characteristics similar to those of type II benzodiazepine receptors but has a markedly lower affinity for zolpidem and CL 218872 than other type II receptors. These studies suggest that type II benzodiazepine receptors are likely to be heterogeneous and that receptor subunit composition may play an important role in determining regional differences in benzodiazepine sensitivity.

A model of GABA$_A$ receptor structure and function can be proposed from the combination of molecular biological and biophysical studies (see figure 2). The receptor is likely a pentamer comprising α-, β-, and γ-subunits, each of which is a glycoprotein with four transmembrane-spanning regions. The final functional properties of the receptor, including agonist affinity, conductance, rate of desensitization, and benzodiazepine sensitivity, are determined by the different subunits constituting the receptor (83). Structural homology between nicotinic receptor subunits and GABA$_A$ receptor subunits suggests that each GABA$_A$ subunit is likely to contribute a single transmembrane segment to the ion channel. The ion channel is selective for chloride under physiological conditions, and this selectivity results from clusters of positive charges within the channel lining with which negatively charged chloride ions interact. Structural studies reveal two such areas of positive charge coinciding with the predictions of biophysicists. Fixed hydroxyl groups within the first and second transmembrane-spanning regions are likely to maintain the water content of the channel and strip the waters of hydration from chloride ions as they traverse the channel (70).

FIGURE 2. Model of the GABA-Benzodiazepine Receptor Complex[a]



[a]Current data suggest a pentameric protein composed of α-, β-, and γ-subunits; the proposed arrangement of subunits is arbitrary. There are two sites for GABA binding (on the β-subunits) and a single site for benzodiazepine (BDZ) binding (depicted on the γ2-subunit). Homology between the GABA$_A$ receptor and the nicotinic acetylcholine receptor suggests that the chloride ion channel is formed by contributions from each subunit.

Several features of GABA$_A$ structure and function are less certain. At present, the role of extracellular glycosylation in ion channel physiology is unclear, but experiments using the glycosylation inhibitor tunicamycin suggest that these sites may be important for imparting the proper tertiary structure for passing ions (84). Additionally, the role of the intracellular phosphorylation sites on the β- and γ-subunits is unclear. Experiments using patch clamp techniques suggest that these sites may be important in maintaining long-term integrity of responses and that phosphorylation may be a means of regulating the function of the complex by other neurotransmitters and second messengers (85, 86). Further support for this idea comes from studies demonstrating that both cAMP-dependent protein kinase and protein kinase C are capable of phosphorylating purified GABA$_A$ β-subunits (87, 88). Other evidence indicates that the α-subunits can be phosphorylated by a receptor-associated protein kinase (89). Finally, analogues of cAMP have been shown to modulate GABA$_A$ responses in cultured hippocampal neurons (90), providing some evidence for a functional consequence of phosphorylation.

It must be emphasized that the current view of the GABA$_A$ complex is hypothetical and based on known biophysics and structure. However, the availability of structural maps complemented by site-directed mutagenesis experiments will allow the proposed model to be examined directly. Similar site-directed experiments with cloned nicotinic acetylcholine receptors have provided insights into the mechanisms of channel action and modulation by various drugs (91).

GABA$_A$ RECEPTORS AND PSYCHIATRY

In the late 1970s, after several studies had linked benzodiazepines to specific receptors in the CNS, it was believed that psychiatry would embark on a new age in drug therapy (92). It was hoped that insights into the chemistry of benzodiazepine receptors would shed light on the mechanism of action of this class of drugs and ultimately on the pathophysiology of anxiety disorders. The receptor story has evolved a great deal in the last 15 years, and the sites of action and cellular mechanisms of benzodiazepines and barbiturates are much better understood. Unfortunately, the pathophysiology of anxiety remains less well defined. The prominent actions of sedative-hypnotics on the GABA$_A$ complex make these proteins leading candidates for sites of pathology in anxiety states. What is less certain is whether these receptors play a role in generalized or "free floating" anxiety or whether they are involved in panic attacks, phobias, or other symptoms accompanying anxiety disorders. The fact that alcohol, benzodiazepines, and barbiturates all affect the GABA complex but only high doses of benzodiazepines have proven effective in the treatment of panic attacks suggests a role for GABA in generalized anxiety and level of arousal (93).

Support for a role of GABA-benzodiazepine receptors in generalized anxiety comes not only from the actions of anxiolytics but also from the actions of benzodiazepine inverse agonists. These agents, which include β-carboline derivatives and the endogenous peptide diazepam-binding inhibitor, have intrinsic pharmacological properties that are the opposite of those of clinically used benzodiazepines (9). These agents produce "anxiogenic" effects in animals—signs of behavioral agitation as well as increases in heart rate, blood pressure, and stress hormones (7). These effects can be blocked or reversed by anxiolytic benzodiazepines. Administration of a β-carboline derivative to human volunteers was similarly accompanied by symptoms of anxiety and elevations of heart rate, blood pressure, and plasma cortisol (94).

It is unlikely that GABA$_A$ receptors represent the only transmitter system involved in the pathophysiology of anxiety. Considerable evidence suggests a role for the noradrenergic system (6) as well as a number of peptides and hormones (7). However, the ubiquity of GABA receptors in the CNS and the known interactions among various transmitter systems make this an attractive system through which symptoms can be manipulated pharmacologically.

The GABA-enhancing actions of alcohol and sedative-hypnotics make this complex a candidate for involvement in the pathophysiology of certain forms of substance abuse (12, 95). At the minimum, features such as drug tolerance and withdrawal are likely to be understood in terms of changes in the flow of ions through GABA$_A$ channels. Tolerance and withdrawal are major concerns regarding benzodiazepine administration, although these drugs clearly have a superior therapeutic index compared with barbiturates. One interesting theory regarding withdrawal is that continued administration of benzodiazepine agonists and inverse agonists is associated with a change in receptor-ionophore coupling (96–98). The effect, described as a "withdrawal shift," is an increase in the intrinsic properties of inverse agonists and a decrease in the properties of agonists. Other evidence suggests a down-regulation of GABA$_A$ receptors during the continued administration of alcohol and benzodiazepines to animals (99, 100) and a compensatory hyperexcitable state on withdrawal of the drugs (99, 101). Functional effects of chronic ethanol exposure on GABA-mediated chloride flux have also been reported (13). In these studies, chronic ethanol administration produced a decrease in muscimol- and pentobarbital-stimulated chloride uptake by rat synaptoneurosomes. Additionally, the ability of ethanol to potentiate GABA responses was lost, suggesting that drug tolerance involves functional changes in the receptor-channel complex. The changes in receptor function were reversible on discontinuation of ethanol. These observations have important implications for understanding the pathophysiology of withdrawal states and suggest that subsensitivity of GABA$_A$ receptors may be responsible for some symptoms. Similar functional changes in chloride flux have also been reported following chronic exposure to benzodiazepines (102), suggesting that the functional mechanisms of tolerance may be similar to those seen with alcohol.

A related but unanswered question concerns whether differences in the GABA$_A$ complex among individuals play a genetic role in the selection of alcohol or sedatives as preferred drugs of abuse. Just as some individuals have a genetic-metabolic inability to tolerate alcohol (103), other individuals may select these drugs because of differences in their neuroreceptors and the related effects on the nervous system. Several reports have documented differences in ethanol-benzodiazepine sensitivity in genetically inbred strains of animals (14). These studies provide tentative support for the hypothesis that differences in CNS function and receptors may underlie differences in drug preference and effects on given individuals. Studies in humans also suggest familial differences in the effects of alcohol (104).

The role of GABA$_A$ receptors in other psychiatric disorders is less clear. The complex relationship between depression and anxiety suggests a role for the receptor in depression, although response to standard benzodiazepine therapy is difficult to distinguish from placebo in clinical trials (105). An alternative to pharmacological methods of considering receptor involvement in psychiatric disorders is to consider receptor subunits as candidate genes for psychiatric disorders with a substantial genetic component. Polymorphisms for receptor subunits and flanking markers can be linked to particular disorders in human pedigrees. This work is facilitated by mapping the chromosomal location of subunit genes. Current work indicates that the GABA α1-subunit maps to human chromosome 5q34-35, the α2- and β1-subunits to 4p12-13, and the α3-subunit to Xq28 (106). Interestingly, this X-chromosome region has been linked to a form of bipolar affective disorder (107), raising the possibility that the α3-subunit gene could be involved in certain forms of the disorder. Other workers (108) reported linkage between a polymorphism in the human coagulation Factor 9 locus (Xq27) and bipolar affective disorder. The maximal lod score was attained 11 centimorgans from the Factor 9 locus, a genetic distance compatible with a role for the α3 gene in the disorder in these families. Uncertainty about the chromosomal location of the disease locus in these families, either toward the centromere, which would be away from the α3 gene, or toward the telomere, which could be close to the α3 gene, makes the relationship less clear. If linkage between the α3-subunit and bipolar disorder can be demonstrated and, even more important, replicated, subsequent efforts would be aimed at defining possible molecular pathology of the α3-subunit at the single base level.

FUTURE DIRECTIONS

The exciting possibilities coming from the current studies are that future understanding of disease states, drug effects, and therapeutic successes and failures may be expressed in terms of differences in the structure and function of specific receptors and their associated ion channels (109). Furthermore, the ability to describe the molecular function of receptor subtypes by expressing the protein in heterologous systems such as frog eggs or transfected cells offers the ability to tailor drug specificity by developing agents directed against a given receptor subtype (110). One example of the power of this approach is seen in observations regarding the location (111) and subunit composition of type I and type II benzodiazepine receptors (81, 82). These observations, coupled with earlier suggestions that type I receptors mediate anxiolytic but not sedative effects of benzodiazepines (42), raise the possibility that receptor-specific therapeutic agents will be developed and perhaps exhibit more favorable side effect profiles. Already, a type-II-selective benzodiazepine, quazepam, has been marketed as a hypnotic agent. Receptor-specific benzodiazepine partial agonists and antagonists represent other classes of drugs with potential clinical utility. Current data indicate that the partial agonists have anxiolytic effects but diminished liability for dependence (112). The antagonists have been shown to block the effects of benzodiazepines and alcohol (52) and may prove useful in reversing drug action in anesthetic and overdose situations (113, 114).

Better definition of the structural elements responsible for drug binding should help in efforts to design more specific therapeutic agents. These developments will be enhanced by elucidation of secondary and tertiary protein structure as might be provided by X-ray crystallographic studies. Other studies using site-directed mutagenesis should provide insights into key areas of the receptor-channel complex that can be modified pharmacologically. It remains to be seen how different subunit composition in various regions of the nervous system alters the gating properties of the $GABA_A$ complex.

The current GABA studies also have important implications for the understanding of how neurotransmitter systems may be involved in illness. Simple notions of increases or decreases in transmitter levels, metabolites, or receptors in a disease state will need to be tempered by an understanding of how such changes may affect each of the receptor subtypes in a given region. It is possible that specific disorders may reflect abnormalities of only a single receptor subtype. Thus, crude measurements of transmitter levels offer little hope of shedding light on pathophysiology. In addition, molecular genetic studies offer the opportunity of directly considering receptor subunit gene involvement in psychiatric disorders. It is also clear from current molecular studies that diversity in receptor subtype is not limited to the $GABA_A$ system but is a feature shared by most transmitter systems. The exciting work described in this review provides a glimpse of techniques that promise to improve understanding of psychiatric disorders and their treatment.

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Persistence and Remission of Depressive Symptoms in Late Life

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Objective: The relation of poor health to the onset of depressive symptoms in late life is well recognized, but little attention has been given to characteristics that might predict persistence or remission of depressive symptoms. In previous analyses the authors found that increasing disability and declining health preceded the emergence of depressive symptoms in older community residents and accounted for 70% of the variance explained by discriminant analyses. The aim of the present analysis was to examine the relevance of changes in health and disability to the persistence of depressive symptoms. Method: A representative sample of 1,855 adults aged 65 or older were assessed with the Center for Epidemiologic Studies Depression Scale at baseline. Twenty-four months later, 1,577 individuals were available for a second assessment of depressive symptoms. The characteristics of the 97 community residents whose depressive symptoms persisted over 24 months were compared to those of the 114 whose symptoms remitted. Results: Changes in health, differences in age, sleep disturbance, and added formal support services accounted for more than 30% of the variance between the persistently depressed and remission groups. Advanced age and worsening health were associated with persistent symptoms, improved health with remission. Conclusions: Previous studies have indicated that untoward changes in health and disability play a major role in the onset of depressive symptoms. These findings show a substantial contribution to chronicity as well.

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Despite extensive epidemiologic study, information regarding the course, characteristics, prevalence, and consequences of depressive disorders in late life remains problematic (1–4). This is particularly troubling if our mental health policy is to maintain older persons in the community and delay or avoid residence in nursing facilities (5). Depressive symptoms, in addition to cognitive impairment and disability, are distinguishing characteristics of older community residents who enter nursing homes (6). Unfortunately, conventional mental health care that might lessen depression is neither acceptable nor accessible to most older adults who might benefit from it (7–10). Without a better understanding of the dynamics and determinants of depressive symptoms in the elderly, both psychiatric nosology and mental health delivery systems will remain far from ideal.

In previous cross-sectional analyses of a representative sample of older adults (11), we found that 17% of 1,855 community respondents were depressed according to the criteria of the Center for Epidemiologic Studies Depression Scale (CES-D) (12). Poor health and disability explained 35% of the total variance and outranked demographic, social support, and

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life event characteristics in their association with depressive symptoms. We recently reported other findings from longitudinal analyses of this same sample (13). Significant levels of depressive symptoms emerged 24 months after baseline in 9% of the individuals who were not initially depressed. Unlike other investigators (14–18), we found that the number of medical conditions, availability of social support, recent undesirable life events, and demographic characteristics, including age, contributed little in distinguishing those with emerging symptoms from those who remained symptom free. However, increasing disability and declining health preceded the emergence of depressive symptoms in many subjects and accounted for 70% of the variance explained by discriminant analyses. The aim of the present analysis was to determine the relevance of changes in health and disability to the persistence of depressive symptoms. Ultimately we seek to identify the determinants of both the onset and course of late-life depressive symptoms and to determine the contribution of depressive symptoms to an older person's loss of independence.

METHOD

Respondents

Our initial respondents were 1,855 elderly persons selected randomly from a representative sample of Medicare recipients residing in a Bronx community. Between 1984 and 1988, a structured interview was conducted with each respondent every 6 months after a comprehensive baseline interview to monitor change in health status and social circumstances. The CES-D was administered at the baseline comprehensive interview and at the 24-month structured interview. Of the initial 1,855 respondents, 278 (15.0%) were not available for the 24-month CES-D assessment because of death, dropping out, or incapacity. Baseline and 24-month CES-D scores were therefore available for 1,577 individuals.

Variables

The initial selection of independent variables was based on findings from our previous studies (6, 11, 13, 19, 20) and those of others (14–18). The categories of variables included health and disability, opportunities for companionship, sociodemographic characteristics, social support, life events, and treatment characteristics that might influence the course of depression, specifically the use of psychotropic medications and visits to mental health specialists.

The CES-D (12) is a series of 20 questions that elicit the frequency of depressive symptoms in the 2 weeks before administration. It correlates well with longer self-report scales (SCL-90) and clinician interview ratings (Hamilton Rating Scale for Depression, Raskin Depression Scale) (21). Although age and gender show measurable effects on interitem correlations, overall the CES-D assesses a comparable dimension of depression in both men and women, young and old (21). The scale ranges from 0 to 60, and respondents who score 16 or higher meet the conventional criteria for a substantial level of depressive symptoms. One-third of the individuals who score 16 or higher have been found to meet research diagnostic criteria for a major depressive disorder, and fewer than 5% who score less than 16 meet those diagnostic criteria (12). Thus, in classifying respondents as depressed, the CES-D specifies a level of symptoms that predicts rather than confirms the presence of a depressive disorder (17, 22).

Measurement of Variation and Change

To control for potential random variations in the CES-D scores above or below 16 during the period from baseline to 24 months, we defined remission as a 24-month score that was both below the 16-point threshold for depression and 5 points or more (0.5 standard deviation) below the baseline score. This procedure ensured a more restricted estimate of remission and reduced the number of individuals classified as having remissions by six. Measures of change in income, number of medical conditions, number of problems with activities of daily living, and number of formal support services were statistically controlled for baseline levels by regression to the mean and by incorporating a residual value as the measure for analysis. The number of undesirable life events other than illness (as defined by the respondent), reports of worsened health, and episodes of serious illness recorded at the 24-month interview were analyzed without modification, since they were not compared with baseline values.

Statistical Analyses

The significance of univariate differences between the persistence and remission groups was evaluated with Student-Newman-Keuls tests for continuous variables and chi-square analysis for the variables that were dichotomous. Stepwise discriminant function analyses were used to identify the multivariate set of characteristics that distinguished the persistently depressed from the remission group (23). We estimated the degree of the association between an independent variable and a dependent variable, simultaneously controlling for other variables in the discriminant set, with the standardized canonical coefficient. The cumulative explanatory power (size of contribution to the variance) of characteristics making up the set was estimated with the average squared canonical correlation (24). Only the variables in the discriminant set that were statistically significant or added 1% or more to the average squared canonical correlation were considered important.

In summary, we applied criteria to remove cases in

TABLE 1. Characteristics of Depressed Elderly Community Residents Whose Symptoms Persisted or Remitted During 24-Month Follow-Up

Characteristic (at follow-up unless stated otherwise)	Symptoms Persisted (N=97)				Symptoms Remitted (N=114)				Significant Difference
	N	%[a]	Mean	SD	N	%[a]	Mean	SD	
Male	15	15.4	—	—	24	21.0	—	—	—
Age (years)	—	—	77.5	7.2	—	—	74.0	5.7	t=4.190, df=219, p=0.001
Married	26	26.8	—	—	34	29.8	—	—	—
Living with spouse	20	20.5	—	—	37	34.3	—	—	—
Jewish	63	64.9	—	—	57	50.0	—	—	$\chi^2=4.16$, df=1, p=0.03
Catholic	27	27.8	—	—	41	35.9	—	—	—
Annual income (dollars)									
Baseline	—	—	10,222	11,098	—	—	9,577	6,009	—
Change	—	—	−206	1,553	—	—	−64	1,008	—
Number of medical conditions									
Baseline	—	—	3.3	2.1	—	—	2.8	1.6	—
Change	—	—	+0.1	0.5	—	—	+0.1	0.5	—
Fair to poor health	69	71.8	—	—	78	68.4	—	—	—
Worsening health	52	53.6	—	—	16	14.0	—	—	$\chi^2=37.66$, df=1, p=0.0001
Serious illness	36	38.7	—	—	23	20.1	—	—	$\chi^2=8.63$, df=1, p=0.003
Improved health	4	4.1	—	—	26	22.8	—	—	$\chi^2=13.94$, df=1, p=0.0001
Number of problems with activities of daily living									
Baseline	—	—	1.2	1.9	—	—	1.1	1.8	—
Change	—	—	+0.9	1.9	—	—	−0.2	1.7	—
Added formal support services	—	—	0.2	1.1	—	—	0.0	0.9	—
Vision or hearing impairment	67	69.0	—	—	78	68.4	—	—	—
Sleep disturbance									
Baseline	88	91.3	—	—	91	80.0	—	—	$\chi^2=3.75$, df=1, p=0.05
24 months	80	85.5	—	—	78	68.4	—	—	$\chi^2=8.78$, df=1, p=0.003
Psychotropic medication	20	20.6	—	—	32	28.0	—	—	—
Mental health visits	8	8.2	—	—	13	11.4	—	—	—

[a] Data not available for all subjects on some items, so number on which percents were based varies.

which changes in CES-D scores over time were statistically insignificant and generated a discriminant analysis using respondent characteristics that we hypothesized would distinguish the persistence and remission groups. The persistence and remission groups were examined not only in relation to baseline characteristics, but also in relation to changes in health, disability, social support, income, and adverse life events between the baseline and 24-month measurements of depression. Our focus on the dynamics of depressive symptoms builds on descriptions of more cross-sectionally defined predictors of depression (13–17).

RESULTS

We found that 1,226 (77.7%) of the respondents were never symptomatic, 140 (8.9%) became symptomatic, and 97 (6.2%) were persistently symptomatic. Remission from a substantial baseline level of depressive symptoms occurred in 114 (7.2%). The prevalence of depressive symptoms declined from 16.9% (313 of 1,855) at baseline to 15.0% (237 of 1,577) 24 months later; the latter figure includes both the newly symptomatic and persistently symptomatic groups. The remission rate was 54% among the 211 respondents who met the CES-D criteria for depression at baseline. The persistently symptomatic and remission groups differed in a variety of ways (table 1). Overall, the respondents with persistent symptoms were older and had higher prevalences of Jewish religious preference, worsening health, serious illness, and sleep disturbance. Improved health was reported by 22.8% of the remission group but only 4.1% of the persistently symptomatic respondents. Gender, marital status, economic status, number of medical conditions, impairments in vision or hearing, self-assessed health, and problems with activities of daily living at baseline did not differ significantly. Neither were there significant differences between the groups in change in the number of medical conditions, change in economic status, or use of psychotropic medications or visits to mental health specialists during the 24-month follow-up period.

In the discriminant function analyses (table 2), differences in age, changes in health, sleep disturbance, and formal support services added since baseline explained 31% of the total variance between the two groups, expressed as the cumulative average squared canonical correlation. Age and changes in health played the largest role in distinguishing the groups. Together these characteristics explained 27% of the total variance and accounted for 85% of the explained

TABLE 2. Stepwise and Canonical Discriminant Analyses of Characteristics Distinguishing Depressed Elderly Community Residents Whose Symptoms Persisted or Remitted During 24-Month Follow-Up

Variable	F (df=1, 199)	p	Average Squared Canonical Correlation	Standardized Canonical Coefficient[a]
Worsening health	48.67	0.0001	0.1918	0.6686
Age	13.28	0.0003	0.2412	0.5134
Improved health	9.14	0.002	0.2739	−0.4533
Sleep disturbance at 24 months	5.58	0.01	0.2935	0.2903
Added formal support services	4.92	0.02	0.3104	0.2504

[a] Group means are 0.6189 for the persistently depressed group and −0.7586 for the remission group. Positive values identify characteristics associated with persistent depression.

variance. The two groups did not differ significantly in the number of baseline medical conditions or change in the number of medical conditions. Similarly, marital status, demographic characteristics, and number of undesirable life events reported for the 6 months preceding the 24-month interview failed to distinguish one group from the other. Our previous examination of respondent deaths and attrition suggests that the relations between the persistence of depressive symptoms and change in health may be greater than revealed by these analyses (13, 20). The mean CES-D score at baseline for the respondents who died during the 24 months of observation was significantly higher than the scores of the dropouts and the respondents who survived. The mean value for dropouts, however, was not significantly different from that of the survivors. Thus, proportionately more of the depressed respondents, whose symptoms might have persisted and who could have reported worsening health, failed to survive for the 24-month interview. Their absence from the discriminant analysis would reduce the ability of that analysis to identify the role of declining health in distinguishing between the study groups. Nonetheless, the group means for the canonical variables were 0.6189 for the persistently depressed and −0.7586 for the recovered respondents, indicating that the study variables achieved a substantial separation of the groups. Furthermore, the group of characteristics correctly identified 66% of the persistently depressed and 84% of the recovered respondents.

DISCUSSION

Roth and Kay (25) were among the first to observe the relation of poor health and disability to the onset of late-life depressive disorders. More recently, community surveys of depressive symptoms, rather than depressive disorders, have consistently demonstrated the same strong relationship of age, poor health, and disability to symptom onset (13–17). Subsequently, little attention has been given to the role of these characteristics in the remission or persistence of depressive symptoms (13–17, 26, 27). The available data are based, like Roth and Kay's, on clinical intervention studies of late-life depressive disorders (28–32). Also, with the exception of Kivela and Pahkala's findings (32), prevalence data from community surveys have been derived from interviews of physically healthy elderly persons (2). The resulting prevalence of depressive disorders may not apply to older adults with depressive symptoms and concomitant physical illness. These individuals represent a substantial minority of the aged population.

Thus, both onset and outcome data that might inform us as to factors associated with the course of depression have been available only from uncommonly healthy community samples or from clinical cohorts followed after the initiation of treatment. In contrast, our study provides information on the course of depressive symptoms in a representative sample of older community residents and is not biased by the selection effects of diagnostic categorization or a specialized treatment program. Over a 24-month interval, significant levels of depressive symptoms persisted in 6.2% of our community sample of older adults and remitted in 7.2%. This represents a recovery rate of 54% among the depressed respondents. It should be kept in mind that symptoms are more labile than diagnosed disorders, so any recovery rate based on symptomatic rather than diagnostic measures must be viewed cautiously. We believe our study is among the first to 1) estimate a remission rate for depressive symptoms in a representative sample of elderly adults who received routine medical care and 2) identify measures of change that predict the chronicity and remission of depressive symptoms. Comparable remission and persistence rates for depressive disorders or depressive symptom clusters in the elderly participants in the Epidemiologic Catchment Area Program or the Established Populations for the Epidemiologic Study of the Elderly are not yet available (33, 34).

Our results indicate that changes in health provide a major if incomplete explanation of the remission or persistence of depressive symptoms. By encompassing both improvement and decline in health, our findings imply that it is the direction of change, as opposed to the level or persistence of illness, that is critical to the course of depressive symptoms. When combined with our previous findings about emerging symptoms of depression, changes in health and independence over 24 months appear to be more important than baseline health status, number of medical conditions, number of problems with activities of daily living, and sociodemographic characteristics in explaining the course of depression. It is not surprising that the use of psychotropic medications and visits to mental health specialists did not distinguish the persistently depressed persons from those who recovered. Only 8% of the persistently depressed and 11% of the remission group had seen mental health specialists. Moreover, the elderly more often receive symptomatic treatment with antianxiety or hypnotic agents rather than definitive treatment with antidepressants. They are less likely to receive adequate initial and maintenance antidepressant therapy. And they are more likely to experience adverse reactions to medication, all of which contribute to the likelihood that depressive symptoms will persist (27–31).

Although much about late-life depressive disorders remains problematic, our survey has helped to clarify certain determinants of the course of late-life depressive symptoms. Changes in health and increasing disability have the preeminent roles in the emergence and persistence of depressive symptoms. Analyses of institutionalization and mortality should demonstrate the extent, if any, that depressive symptoms contribute to a loss of survival in the community, beyond their association with disability and declining health. Previous studies have indicated that poor health and disability play a major role in the onset of depressive symptoms. Our findings demonstrate the substantial contribution of changes in health to chronicity and recovery as well.

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Characterization of Depression in War-Related Posttraumatic Stress Disorder

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Objective: Many patients with posttraumatic stress disorder (PTSD) have symptoms of depression, but operationalized psychological constructs related to depression have not been used extensively in characterizing affective symptoms of PTSD. The authors' objective is to better characterize the affective component of PTSD. Method: The subjects were 45 male psychiatric inpatients at a Veterans Administration medical center; 28 met DSM-III-R *criteria for PTSD and 17 met Research Diagnostic Criteria (RDC) for major depressive disorder. All of the subjects with PTSD were Vietnam veterans. The 21-item Hamilton Rating Scale for Depression was used to assess state measures of symptom severity, and the Depressive Experiences Questionnaire was used to measure dimensions of dependency, self-criticism, and self-efficacy. Results: The mean total Hamilton scale score of the patients with PTSD was nonsignificantly higher than that of the patients with major depressive disorder; patients with PTSD had higher scores on almost all individual Hamilton symptoms, particularly insomnia, somatic anxiety, and diurnal variation. Patients with PTSD had significantly higher scores on the self-criticism scale but not on the dependency and self-efficacy scales of the Depressive Experiences Questionnaire. The scores of patients with PTSD on the dependency and self-criticism scales were negatively correlated. No significant differences between patients with PTSD with and without concurrent major depressive disorder were observed. Conclusions: Characterization of such depressive dimensions of PTSD as dependency and self-criticism may have important clinical implications.*

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Many combat veterans with war-related posttraumatic stress disorder (PTSD) report feeling depressed or have depression-related symptoms such as sleep disturbance, social withdrawal, suicidal ideation, decreased appetite, and low self-esteem (1–4). In fact, a substantial proportion of combat veterans with PTSD meet the full *DSM-III* or *DSM-III-R* criteria for dysthymia (5, 6) or major depressive disorder (7, 8).

Despite high rates of depression in PTSD, antidepressants as well as psychotherapeutic approaches targeted at reducing affective distress are not as effective in depressed patients with PTSD as they are in patients who have major depressive disorder without PTSD (5, 6, 9–12), suggesting that the nature of depression in PTSD differs from that in major depressive disorder. Further support for this idea comes from biological studies that have demonstrated marked neuroendocrinological differences between PTSD and major depressive disorder (13–15). It appears, then, that depressive symptoms in PTSD, although frequent, are not simply manifestations of a concurrent major depressive disorder. Rather, the depressive component of PTSD may reflect either secondary, characterologic, or atypical depressions, and as such may require different treatment interventions. For example, various subtypes of depression without PTSD have differential responses to treatment: some are more responsive to medications and others to psychotherapy.

To date, the phenomenology of depression in patients with PTSD has been studied by using primarily descriptive symptom assessment. Operationalized psychological constructs related to depression have not been used extensively in characterizing affective symptoms of PTSD. To better characterize the affective component of PTSD, we assessed not only diagnostic and state measures of depression using the Schedule

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for Affective Disorders and Schizophrenia (SADS) (16) and the Hamilton Rating Scale for Depression (17) but also subjective experiences thought to reflect more enduring dimensions of depression. Specifically, we measured dimensions of dependency (anaclitic), self-criticism (introjective), and self-efficacy using the Depressive Experiences Questionnaire (18).

METHOD

The subjects for the study were consecutively admitted male psychiatric inpatients at a Veterans Administration medical center who met *DSM-III-R* criteria for PTSD and/or Research Diagnostic Criteria (RDC) for major depressive disorder and who provided written informed consent to their participation. All subjects with PTSD were Vietnam veterans. PTSD was assessed by using the Structured Clinical Interview for DSM-III-R (SCID) (19). RDC diagnoses for major depressive disorder were made by using the SADS. Patients with schizophrenia, schizoaffective disorder, organic disorder, anxiety disorder, and antisocial personality disorder were not included in the group with major depressive disorder. Patients with borderline personality disorder (assessed by using clinical ratings based on *DSM-III-R* criteria) were also excluded from the group with major depressive disorder. The final study group consisted of 45 subjects: 28 patients with PTSD and 17 with major depressive disorder.

Patients completed the Depressive Experiences Questionnaire within the first 2 weeks of hospitalization. The Depressive Experiences Questionnaire is a 66-item questionnaire that measures the respondent's subjective feelings about himself and about relationships with others. These feelings are thought to be relevant to depression despite the fact that they are not overt symptoms of depression per se. Three highly stable scales on this questionnaire, dependency, self-criticism, and self-efficacy, have been identified in several independent samples (18, 20). Following completion of the Depressive Experiences Questionnaire, the 21-item Hamilton Rating Scale for Depression was administered by an experienced clinician for the purpose of determining more objective, state depressive symptoms. Diagnostic interviews (the SADS and the SCID) took place within 1 month of this evaluation.

Responses of the patients with PTSD and the patients with major depressive disorder on both the Hamilton scale and the Depressive Experiences Questionnaire were tabulated, and differences in means were analyzed by using Student's t test, two-tailed. The patients with PTSD were also subdivided into those who did or did not meet criteria for a concurrent major depressive disorder; the means of these two groups were compared by using the t test. Relationships between Depressive Experiences Questionnaire scores and Hamilton scale scores were determined by using Pearson's correlation coefficient.

TABLE 1. Scores on the Hamilton Rating Scale for Depression of Patients With PTSD and Patients With Major Depressive Disorder

	Patients With PTSD (N=28)		Patients With Major Depressive Disorder (N=17)		t
Hamilton Scale Item	Mean	SD	Mean	SD	(df=43)
Somatic anxiety	1.83	1.15	0.50	1.00	3.37[a]
Insomnia	4.56	1.08	3.33	2.01	2.37[b]
Insight	1.22	1.00	1.92	0.29	−2.36[b]
Diurnal variation	2.35	1.61	1.00	1.60	2.35[b]
Hypochondriasis	0.78	1.08	0.17	0.39	1.89[b]
Psychic anxiety	2.13	1.01	1.42	1.24	1.83[b]
Libido	0.56	0.94	0.25	0.45	1.09
Depersonalization	0.74	1.21	0.17	0.39	1.58
Guilt	2.09	1.12	1.50	0.90	1.56
Suicide	1.61	1.23	1.00	0.85	1.52
Paranoia	0.91	0.87	0.50	0.67	1.41
Somatic gastrointestinal symptoms	0.65	0.88	0.25	0.62	1.40
Agitation	1.04	1.11	0.58	0.90	1.24
Retardation	0.39	0.65	0.58	0.79	0.76
Functional impairment	2.39	1.16	2.17	1.40	0.51
Weight loss	0.43	0.66	0.33	0.65	0.43
Obsessive-compulsive	0.32	0.57	0.25	0.62	0.32
Depressed mood	2.30	1.29	2.33	1.50	0.06
Total	28.42	9.90	24.33	6.30	1.29

[a] Significant difference between groups ($p<0.05$ after Bonferroni correction applied).

[b] Nonsignificant trend for a difference between groups ($p<0.10$).

RESULTS

Patients with major depressive disorder were significantly older than those with PTSD (47.5±14.0 years versus 40.3±5.6 years, respectively; $t=2.36$, $df=43$, $p<0.03$). However, correlational analysis failed to reveal any relationship between age and Hamilton scale scores or scores on any of the Depressive Experiences Questionnaire scales. The two groups were similar with respect to demographic factors such as race, marital status, and socioeconomic status.

The mean total Hamilton scale score for patients with PTSD was 17% higher than that for the patients with major depressive disorder; this difference was not statistically significant (see table 1). Results of individual item analysis revealed that patients with PTSD had slightly higher scores on almost all individual symptoms, particularly insomnia, somatic anxiety, diurnal variation, and, to a lesser extent, psychic anxiety and hypochondriasis.

Analysis of the three Depressive Experiences Questionnaire scales revealed that patients with PTSD had significantly higher scores on the self-criticism scale than did patients with major depressive disorder ($t=2.24$, $df=43$, $p<0.05$). No significant differences were observed on the dependency ($t=0.34$, $df=43$, n.s.) and self-efficacy ($t=0.54$, $df=43$, n.s.) scales. The three scales also appeared to measure three distinct dimensions; i.e., there were no correlations between scores on these scales when the entire study group was considered, nor were any significant correlations observed in the patients with major depressive disorder. When patients with PTSD were considered separately, however, scores on the dependency and self-criticism scales were found to be negatively correlated ($r=-0.47$, $df=27$, $p<0.01$).

To determine the extent to which the overall group differences observed were due to the superimposition of a major depressive disorder on PTSD, we subdivided the patients with PTSD into those with (N=15) and those without (N=13) major depressive disorder. The mean total Hamilton score for patients with PTSD and concurrent major depressive disorder was a nonsignificant 27% higher than that of patients with PTSD without concurrent major depressive disorder. However, results of individual item analyses revealed that patients with PTSD and concurrent major depressive disorder had slightly higher scores on most of the individual items. These 15 patients showed nonsignificant trends for higher scores only on suicidality and insight. Importantly, no significant differences between patients with PTSD with and without concurrent major depressive disorder were observed on any of the three Depressive Experiences Questionnaire scales. The scores of the patients with PTSD with and without concurrent major depressive disorder were 0.39 ± 0.82 versus -0.18 ± 1.3, 1.43 ± 0.79 versus 1.39 ± 0.80, and -0.35 ± 1.2 versus -0.46 ± 1.6 on dependency, self-criticism, and self-efficacy scales, respectively.

DISCUSSION

Our results suggest both similarities and differences in the affective component of PTSD compared with major depressive disorder. Patients with PTSD and patients with major depressive disorder were comparable with respect to overall severity of depression, generally in the moderate to severe range, as indicated by similar overall Hamilton scale scores. Both groups showed similar scores on the dependency and self-efficacy scales of the Depressive Experiences Questionnaire. However, differences in specific Hamilton scale items were observed between patients with PTSD and patients with major depressive disorder. Moreover, patients with PTSD had significantly higher scores on the self-criticism scale of the Depressive Experiences Questionnaire.

Patients with PTSD scored significantly higher on the Hamilton item of somatic anxiety and showed nonsignificant trends for higher scores on insomnia, diurnal variation, psychic anxiety, and hypochondriasis. However, higher scores on these specific items may be related to PTSD symptoms rather than measuring the affective component of the disorder per se. For example, it is well-known that severely traumatized individuals frequently complain of marked insomnia, which may be related to the occurrence of nightmares (21, 22). A greater amount of somatic anxiety may be related to the increased arousal symptoms in PTSD. These symptoms and the trend toward significantly higher scores on psychic anxiety are consistent with the *DSM-III-R* classification of PTSD as an anxiety disorder. Additionally, hypochondriacal fixation, although not a specific PTSD symptom, has been found to be related to combat traumatization (23). Nonetheless, it is important to note that all other depressive symptoms that are unrelated to the presence of an anxiety disorder, including depressed mood, were equally endorsed by patients with PTSD and patients with major depressive disorder. Furthermore, when the patients with PTSD were subdivided into those with and those without major depressive disorder, the patients with PTSD alone still demonstrated a level of depression comparable to that of the inpatients with major depressive disorder without PTSD. The fact that patients with PTSD and concurrent major depressive disorder were significantly more suicidal may be important from a clinical perspective.

The Depressive Experiences Questionnaire measures more subjective, enduring dimensions of depression by asking about life experiences rather than symptoms. Specifically, two types of depression are thought to be identifiable with this instrument: an anaclitic, dependent type where the individual feels helpless and weak, fears abandonment, and longs for protection and love; and an introjective or guilty type of depression where the individual is highly self-critical and feels worthless, guilty, and inferior (24).

Patients with PTSD and patients with major depressive disorder were not significantly different on the anaclitic scale in this study. However, both groups of patients had substantially higher scores than those reported by Blatt et al. (18) for depressed hospitalized male psychiatric patients in the same geographic area who were not war veterans. This finding raises the possibility that psychiatric inpatients who are war veterans are more dependent in general than psychiatric patients who are not war veterans. In contrast, the patients with PTSD had significantly higher scores on the self-criticism scale than did hospitalized patients who were not war veterans (18). It appears that for many combat veterans with PTSD an overwhelming sense of self-criticism and guilt may play a central role in their depression.

The guilt experienced by patients with PTSD may have many sources related to actions and feelings experienced in response to war trauma (25). The present findings in Vietnam veterans suggest that guilt and self-criticism in patients with PTSD may be even more pervasive and nonspecific, affecting multiple areas of life rather than just those related to their experiences in Vietnam. The introjective scale of the Depressive Experiences Questionnaire, for example, contains items like, "I often find that I don't live up to my own standards and ideals" and, "Often I feel that I have disappointed others." Thus, it may be that after years of feeling guilty about experiences in Vietnam, some veterans with PTSD begin to generalize these feelings to other areas of their lives and even to their view of self.

Interestingly, among the patients with PTSD, there was a significant negative correlation between scores on the dependency scale and scores on the self-criticism scale. This was not the case among the patients with major depressive disorder. Examination of the data revealed that the four patients with the highest scores on the dependency scale had the lowest scores on the self-criticism scale, and two of the four patients with the lowest scores on the dependency scale had the highest scores on the self-criticism scale. This relationship led us to examine informally the clinical characteristics of patients scoring in the extreme ranges. Our clinical impression is that many of the patients with the highest scores on the anaclitic scale are deeply invested in their identities as Vietnam veterans. They tend to dress in Vietnam-related clothing with multiple medals and reminders of the war. Many are strongly committed to their fellow Vietnam veterans and find much support from belonging to a closely knit group. Adherence to the group may have helped to protect against fears of abandonment and satisfy wishes to be cared for and protected. Veterans with low scores on the anaclitic scale, however, seemed less invested in their identities as Vietnam veterans and less attached specifically to groups of other such veterans. It is possible that the more anaclitically predisposed recruit had a greater tendency to incorporate a military identity while in the service. It is also possible that some soldiers experiencing massive trauma become increasingly anaclitic and preoccupied with loss and mechanisms to prevent loss.

It appears that there may be a particularly troubled and depressed subgroup of patients with PTSD who scored relatively high on both dependency and self-criticism scales. These veterans seemed both deeply invested in the identity of Vietnam veterans and markedly distressed by their sense of guilt and self-criticism. As noted by one veteran with high scores on both scales, "I love being with my Vietnam brothers. Without them I don't know where I would be. They are the only ones who hold me up when I'm down." The same patient, however, reported an exacerbation of symptoms such as flashbacks and nightmares whenever he increased his participation in Vietnam veteran groups. As he put it, "It's like I can't win. I really love being with these guys, but it reminds me too much of all the bad stuff, and I start getting the nightmares." Blatt et al. (18) found that nonveteran psychiatric patients with high scores on both dependency and self-criticism scales also had particularly severe forms of depression.

Characterization of depressive dimensions of PTSD such as dependency and self-criticism may have important clinical implications. For the individual who is highly anaclitic and invested in his identity as a Vietnam veteran, requests for treatment in a specialized PTSD program may in fact confirm or solidify this basic identity rather than rid the self of the aftereffects of Vietnam. When this is the case, attempts to rapidly reduce PTSD symptoms may fail. In these cases, it may make more sense to help the individual to channel his identity as a Vietnam veteran in a constructive direction. Highly introjective patients, however, may be more amenable to therapies aimed at removing long-standing war-related preoccupations, memories, and symptoms. On the basis of more precise characterization of subtypes and dimensions of depression in patients with PTSD, it may then be possible to develop more specific psychotherapeutic and psychopharmacological interventions.

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Familial Alcoholism in Primary Unipolar Major Depressive Disorder

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Objective: Some studies have suggested relationships between depression in probands and alcoholism in relatives. Other studies have not, but some of these have used inappropriate control groups or failed to divide probands by sex. Method: The present study controlled for sex of probands and used several comparison groups to further explore the familial relationship between depression and alcoholism. Diagnoses for 723 directly interviewed relatives of 326 probands with primary unipolar depression were compared to diagnoses in 469 control subjects chosen by an acquaintanceship method to demographically resemble the relatives of affective disorder probands. Diagnoses in the uninterviewed relatives of both control and depressed subjects were used for comparisons as well. Results: Results indicated higher rates of alcoholism in the families of depressed women but not in the families of depressed men. Conclusions: This familial association between alcoholism and depression may be the result of either genetic or environmental factors or an interaction between the two.

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Many studies show a high rate of familial depression in unipolar primary affective disorder, but there is reason to predict that in a study of patients with primary unipolar depression, one may also find a high rate of familial alcoholism (1, 2). Female depressed patients with a family history of alcoholism are more likely than other depressed patients to have a stormy lifestyle with marital and sexual problems, unstable personality traits, and nonsuppressor status on the dexamethasone suppression test (3). However, not all research has found a high rate of alcoholism in families of female depressed patients (4–6).

One may make the following predictions. If a large proportion of patients with primary unipolar depression have a family history of alcoholism, a comparison of patients with primary depression and a nondepressed control group should show an excess of alcoholism in the family members of the former. In a prior study of 45 depressed probands, male relatives of female probands were more likely to be alcoholic than were male relatives of male probands (7.5% versus 4.6% [7]). Therefore, we would predict that the higher rate of familial alcoholism in depressed than control subjects should be larger in the female proband group than in the male proband group. Similarly, the rate of familial alcoholism should be higher in women with unipolar depression than in men with unipolar depression. These are testable hypotheses, and the National Institute of Mental Health Collaborative Depression Study has collected the kind of data that allow us to evaluate them. Positive findings would support the idea that some proportion of primary unipolar depression is familially related to alcoholism.

METHOD

The probands in this study were collected at five participating centers (Harvard University, Columbia University, Rush Medical College, Washington University School of Medicine, and the University of Iowa College of Medicine). The probands were consecutively admitted hospital patients and newly evaluated subjects in the outpatient clinics. They were required to meet criteria for schizoaffective disorder, bipolar depressive disorder, bipolar I disorder, bipolar II disorder, or unipolar major depressive disorder (primary or secondary subtypes). Having met inclusion criteria, the patients were then interviewed with the Schedule for Affective Disorders and Schizophrenia (SADS) (8). Diagnoses were made according to the Research Diagnostic Criteria (RDC) (9).

The subset of probands selected for this study met criteria for primary unipolar depressive illness. None

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TABLE 1. Alcoholism in First-Degree Relatives of Female Probands With Primary Unipolar Major Depression, in Control Subjects Matched to Subset of Probands' Relatives,[a] and in Probands in Psychosocial Substudy and Matched Control Subjects

	Probands' Relatives/Families			Control Subjects or Their Relatives/ Families			Chi-Square Analysis			
	Total	Alcoholism		Total	Alcoholism					95% Confidence
Comparison	N	N	%	N	N	%	χ^2 (df=1)	p	Odds Ratio	Limits
Family study										
All probands' relatives versus all relative control subjects	477	64	13.4	469	41	8.7	5.24	0.02	1.62	1.07–2.45
Probands' relatives who were matched with control subjects versus relative control subjects	122	18	14.8	122	12	9.8	1.37	0.24	1.59	0.73–3.45
Family history data										
Probands' families versus families of female relative control subjects[b]	210	89	42.4	299	94	31.4	6.42	0.01	1.60	1.11–2.32
Psychosocial substudy										
Probands' relatives versus relatives of psychosocial control subjects	260	33	12.7	220	18	8.2	2.55	0.11	1.63	0.89–2.99
Probands' families versus families of psychosocial control subjects[b]	32	20	62.5	32	13	40.6	3.07	0.08	2.44	0.89–6.65
Relative control subjects rematched to probands[c]										
Probands' relatives versus control subjects' relatives	1,443	148	10.3	1,467	108	7.4	7.60	0.006	1.44	1.10–1.86
Probands' families versus control subjects' families[b]	210	89	42.4	210	71	33.8	3.27	0.07	1.44	0.97–2.14

[a] Control subjects matched to relatives on sex, age, and marital status.
[b] Families compared on presence of alcoholism in family.
[c] Control subjects rematched to probands (originally matched to relatives) on sex, age, and marital status.

had ever received a diagnosis of alcoholism. Family history data on all first-degree relatives both living and dead were collected by using the Family History (FH)-RDC. These data were obtained by interviewing the proband and an informant to produce a consensus diagnosis for each member of the proband's family. This approach does not duplicate family study material obtained through direct interviews with relatives, but it has respectable sensitivity for the major diagnoses when broad but well-specified criteria are used. In particular, the specificity for alcoholism is 96%. In addition to providing family history information, probands were asked to participate in a family study. Relatives of the consenting probands were interviewed by using the SADS-L (Lifetime Version), and a diagnosis was made according to the same criteria as those used for the probands, the RDC. The methodologies of the family history and family study segments of the Collaborative Depression Study have been presented at length in previous reports (10–12).

There were two control groups in the Collaborative Depression Study. The relative control subjects (N=469) were matched to a subset of first-degree relatives directly interviewed as a part of the family study. Each relative provided the names of three acquaintances of similar age, sex, and socioeconomic status. These people were contacted in random order until a willing subject was identified. There were no exclusion criteria. The control subjects were evaluated with the SADS-L, and family history information on their first-degree relatives was collected with the FH-RDC. This acquaintanceship method yielded a control group that tended to be somewhat younger and contained more women than the total sample of interviewed relatives. However, there was no evidence of assortative acquaintanceship by presence or absence of lifetime or current mental disorder in this group.

The psychosocial control subjects (N=108) were matched to a group of probands as part of a psychosocial substudy designed to compare the course of psychosocial events in the control subjects and the depressed psychosocial probands. The control subjects were identical to the probands in age, sex, and marital status. They were evaluated with the SADS-L and were included in the sample only if they showed no history of psychiatric illness. The FH-RDC was used to obtain family history data on the psychosocial control subjects' first-degree relatives.

Comparisons of familial alcoholism in the proband and control groups were tested for significant differences by use of chi square with one degree of freedom. A two-tailed test at the 0.05 level of probability was considered significant.

The odds ratios for the comparisons are presented in order to show the magnitude of the differences. The 95% confidence limits are also presented. The odds ratios are useful because some differences are of similar magnitude but do not reach significance because of small numbers. "The odds ratio is also termed the cross product ratio and the approximate relative

TABLE 2. Alcoholism in First-Degree Relatives of Male Probands With Primary Unipolar Major Depression, in Control Subjects Matched to Subset of Probands' Relatives,[a] and in Probands in Psychosocial Substudy and Matched Control Subjects

Comparison	Probands' Relatives/Families			Control Subjects or Their Relatives/ Families			Chi-Square Analysis		Odds Ratio	95% Confidence Limits
	Total N	Alcoholism N	Alcoholism %	Total N	Alcoholism N	Alcoholism %	χ^2 (df=1)	p		
Family study										
All probands' relatives versus all relative control subjects	246	29	11.8	469	41	8.7	1.70	0.19	1.40	0.84–2.31
Probands' relatives who were matched with control subjects versus relative control subjects	53	4	7.5	53	4	7.5	0.00	1.00	1.00	0.24–4.23
Family history data										
Probands' families versus families of male relative control subjects[b]	116	31	26.7	170	42	24.7	0.15	0.70	1.11	0.65–1.91
Psychosocial substudy										
Probands' relatives versus relatives of psychosocial control subjects	153	5	3.3	158	12	7.6	2.82	0.93	0.41	0.14–1.20
Probands' families versus families of psychosocial control subjects[b]	25	4	16.0	25	10	40.0	3.57	0.06	0.29	0.88–1.09
Relative control subjects rematched to probands[c]										
Probands' relatives versus control subjects' relatives	702	44	6.3	759	47	6.2	0.00	0.95	1.01	0.66–1.55
Probands' families versus control subjects' families[b]	116	31	26.7	116	35	30.2	0.34	0.56	0.84	0.48–1.49

[a] Control subjects matched to relatives on sex, age, and marital status.

[b] Families compared on presence of alcoholism in family.

[c] Control subjects rematched to probands (originally matched to relatives) on sex, age, and marital status.

risk. . . ." This method is useful in providing an idea of the order of magnitude of the proportions from a comparison of two groups (13). The odds ratio is defined as the odds of alcoholism in relatives of depressed subjects compared to the odds of alcoholism in relatives of control subjects.

RESULTS

Table 1 presents seven comparisons between family members of primary depressed female probands and control subjects. Multiple comparisons are presented in order to obtain an idea of the consistency of the findings when we vary the composition of the proband and comparison groups. This is necessary as we have used two different methodologies, a family study method (personal information) and a family history method that depends on information gleaned from information of other relatives. We have compared alcoholism in individuals and also the presence or absence of alcoholism in families. The family comparisons are useful because there is some question about the independence of comparing alcoholism in people who are related to each other, i.e., the data suggest that if families contain one alcoholic they are more likely to contain another person with alcoholism than would be expected by chance. Thus, there may be a spuriously high rate of alcoholism found by dealing with individuals rather than by dealing with the presence or absence of alcoholism in a family. The comparison of proportion of families that have alcoholism is a more conservative method than a comparison of the prevalence of alcoholism in individuals of two groups.

The first two rows (table 1) deal with the family study. The first row is a comparison of all the relative control subjects (male+female) versus the interviewed first-degree relatives of the primary unipolar probands. The control subjects were not directly matched to these relatives.

The second row is a comparison of only the relatives of female probands who originally had matched control subjects versus these control subjects. In table 2, there are similar kinds of comparisons for the relatives of male probands and the control subjects.

The family history data comprises the material for the third–seventh rows. These data were obtained from the FH-RDC evaluations of the probands, relative control subjects, and psychosocial control subjects. The third row compares the families of all female relative control subjects with the families of female probands. Table 2 does the same thing for male control subjects and probands. The fourth row compares the relatives of the 32 unipolar women in the psychosocial study to the relatives of their matched psychosocial control subjects (table 1). Table 2 does the same for men. The fifth row presents the same comparison as row 4 but looks at the presence of alcoholism in families rather than in individual relatives. The sixth and seventh rows are somewhat more complex. In these cases the relative control subjects were rematched to the probands, and the relatives of the control subjects were compared to the relatives of the probands (row 6). Then, families of the control subjects were compared to the families of the probands (row 7).

In the case of all the comparisons in rows 2–7, the two groups were matched on sex, age, and marital status.

None of the comparisons in table 2, which presents data on alcoholism in first-degree relatives of men with primary unipolar major depression and in control subjects, is significantly different. Further, the odds ratios are clearly smaller (in seven of seven cases) than those in table 1. In table 1 comparisons in the first, third, and sixth rows show significant differences between the two groups. In those which do not show significant differences at the 0.05 level or better, the odds ratios are of the same magnitude. All seven of the comparisons in women (table 1) are in favor of more alcoholism in families of probands than in families of control subjects, and it is important to note that the trends are exactly in the predicted direction and the odds ratios vary between 1.4 and 2.4.

We also compared the presence of alcoholism in families of men and women with unipolar depression. There was a significant difference, with women having more familial alcoholism than men (89 of 210 families [42.2%] versus 31 of 116 families [26.7%]; $\chi^2=7.88$, df=1, p=0.005; odds ratio=2.02; 95% confidence limits=1.24–3.29).

DISCUSSION

We tested the hypothesis that there is a familial relationship between alcoholism and primary depression. In particular, we predicted that the relatives of women with primary depression would have higher rates of alcoholism than would control subjects. Although many depressed patients have no family history of alcoholism and thus do not have this subtype of depression, this condition apparently occurs with sufficient frequency to consistently produce the differences predicted here. If certain subjects with primary depression have a family history of alcoholism, we would expect a higher rate of alcoholism in the families of such subjects. It was predicted that there would be such a relationship for women with primary depression and that we would be able to arrive at this by finding a higher rate of familial alcoholism in this group than in control groups. Most depressed subjects have no family history of alcoholism, but if some proportion did, the prevalence would be consistent and significant; this was found.

This hypothesis has been tested by others, not always with positive results. Gershon et al. (4) conducted a family study of affectively ill and normal control probands. They concluded that alcoholism was not more frequent in the relatives of patients than in the relatives of control subjects. The lifetime risk for alcoholism was 6.6% in relatives of 166 subjects with unipolar depression and 4.2% in relatives of 265 control subjects. Although there was 50% more alcoholism in the families of subjects with unipolar depression, this is an insignificant finding. However, in that study the patients were not separated into groups of men and women with primary unipolar depression. Thus, the present study and the study by Gershon et al. are not comparable.

Weissman et al. also looked at this phenomenon (5). They found that the prevalence of alcoholism was 7.6% to 10.5% among relatives of severely depressed probands, 12.2% among relatives of mildly depressed probands, and 7.9% among the relatives of normal control subjects. These are not significant differences. The authors stated that alcohol abuse does "not show familial aggregation with affective disorders." Depressed women were not evaluated separately.

Merikangas et al. (6) found more alcoholism in relatives of depressed subjects, but this was accounted for by the presence of alcoholism as well as depression in some probands. Our female probands, however, did not have a concomitant diagnosis of alcoholism, and so the findings conflict. As in the other studies, depressed women were not evaluated separately.

Cloninger et al. (14) evaluated a variety of data sets and concluded that alcoholism and depressive illness sometimes appear in the same family but that these disorders are probably heterogeneous etiologically and are not simply expressions of underlying genetic mechanisms. They noted that subjects with primary depression had fewer alcoholic relatives than did nondepressed alcoholics. This would be expected if only a proportion of depressed subjects were related to an alcoholic background. In one study (15), 17% of hospitalized depressed patients had a first-degree relative with a history of alcoholism. Cloninger et al. presented general population prevalence data for primary alcoholism (4.8%). If one compares this prevalence with that of alcoholism in personally examined first-degree relatives of subjects with early-onset depression (11%), the difference is significant (p<0.01). As these assessments were obtained from different populations and with different methodologies, such comparisons are probably unwarranted. The data from the current study, however, were collected with the same methodology for control subjects and relatives.

Finally, if these data are valid, they suggest that there is a particular type of depression which may be associated with a family background of alcoholism.

There are some clinical, follow-up, laboratory differences in the subgroups of depression (1, 2). The depression of a person with a family history of alcoholism starts when the person is in his or her early 30s and is manifested after a stormy personal life marked by marital and social difficulties. The dexamethasone suppression test shows abnormal suppression less commonly in these patients than in those with no family history of alcoholism (16).

A familial history of alcoholism may or may not be related to genetic factors. Two separate linkage studies suggest a genetic association between alcoholism and depression, but these data are not strong enough to prove a genetic etiology (17, 18). It is possible that interaction between genetic and environmental factors is involved in the familial relationship. Other possible explanations for the finding might include assortative mating or an environmental factor that might be related to the influence of living with an alcoholic.

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Less Frequent Lithium Administration and Lower Urine Volume

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Objective: This study was designed to determine whether patients maintained on a regimen of lithium on a once-per-day schedule have lower urine volumes than do patients receiving multiple doses per day. Method: This was a cross-sectional study of 85 patients from a lithium clinic who received different dose schedules. Patients were admitted to the hospital for measurement of lithium level, creatinine clearance, urine volume, and maximum osmolality. Results: Multiple daily doses of lithium were associated with higher urine volumes. The dosing schedule, duration of lithium treatment, and daily dose of lithium did not affect maximum osmolality or creatinine clearance. Conclusions: Urine volume can be reduced by giving lithium once daily and/or by lowering the total daily dose. Lithium-induced polyuria seems to be related to extrarenal as well as to renal effects.

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One of the major concerns about the long-term use of lithium has centered around the issue of possible detrimental effects on the kidney. In this connection, polyuria has been considered an important indicator of renal tubular changes. Findings that have contributed to this concern are 1) consistent reports that a proportion of patients receiving long-term lithium treatment develop polyuria (1, 2), 2) the fact that polyuria is correlated with duration of lithium treatment and with higher doses of lithium in some studies (1, 2), and 3) the fact that renal concentrating ability is decreased in some patients with lithium-induced polyuria and is usually but not always ameliorated within a few months after discontinuation of lithium (1–4). Even though some degree of polyuria is not dangerous by itself, dehydration that may result from polyuria could predispose the patient to lithium toxicity.

Studies of groups of patients from different clinics and within the same clinic have found that those patients who took lithium once per day had significantly lower urine volumes than those who took lithium twice per day (5, 6). Studies by Plenge et al. in 1982 (6) and Hetmar et al. in 1987 (7), which compared patients receiving single and multiple daily doses of lithium, found more sclerotic glomeruli, fibrosis, and atrophic tubules in the kidneys of patients on the multiple dose schedule. In these studies patients receiving the multiple dose schedule received a higher total daily dose of lithium (6, 7). This variable was controlled for in a study in which eight patients were switched from a twice-daily schedule to a once-daily schedule but received the same total daily dose (8). The 24-hour urine volume fell significantly after 12 days of the single dose—from a mean±SD of 2,105±949 ml to 1,566±974 ml (8).

Not all studies have found a correlation between duration of lithium treatment and urine volume (9). Those studies that have found a positive correlation included in their samples a high proportion of patients with polyuria or reduced maximum urinary concentrating ability (3, 10–12). This limits the generalizability of their findings. Most studies did not correct for age, an important point since concentrating capacity decreases with age, and, naturally, the duration of treatment tends to increase with increasing age (3, 11, 12). Sex, but not the unipolar/bipolar distinction, has been found to be associated with urine volume in patients receiving lithium (9).

In our study, data from patients in a lithium clinic, where various dose schedules have been used, provided an opportunity to examine the effect of dose schedule on urine volume, creatinine clearance, and maximum osmolality.

METHOD

The subjects were 85 consecutively studied patients receiving long-term lithium treatment from a McMas-

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TABLE 1. Characteristics of 85 Patients Who Received Lithium Once, Twice, or Multiple Times Daily for More Than 1 Year

Daily Dose Schedule of Lithium	Age (years)			Length of Treatment^a (months)			Dose (mg/24 hours)			Serum Lithium Level (mmol/liter)		
	Mean	SD	Confidence Interval	Mean	SD	Confidence Interval	Mean	SD	Confidence Interval	Mean	SD	Confidence Interval
Once (N=26)	46.0	11.2	41.5–50.6	62.7	36.1	48.1–77.3	980.8	244.6	882.0–1079.6	0.83	0.18	0.75–0.90
Twice (N=42)	53.9	14.7	49.2–58.4	82.2	33.6	71.7–92.7	1167.9	343.6	1068.8–1274.9	0.77	0.18	0.72–0.83
Multiple (3 or 4 times) (N=17)	51.6	13.7	44.5–58.6	47.3	29.9	31.9–62.7	1085.3	345.9	907.5–1263.1	0.78	0.14	0.71–0.85

[a] $F=7.19$, df=2, 82, $p<0.01$ (ANOVA).

[b] $F=3.00$, df=2, 79, $p<0.05$ (ANCOVA with age, sex, length of treatment, and daily dose as covariates). There was a significant difference at the 0.05 level between the urine volumes of patients given lithium once daily and patients given lithium multiple times daily (Duncan's multiple range test).

[c] Geometric means.

ter University affective disorders clinic. This was a representative group of patients in the clinic, since during the period of study only one patient did not consent to testing. The patients had taken lithium for an average of 6 years and for a minimum of 1 year and had been maintained at an average serum lithium level of 0.79 mmol/liter. None of the patients had ever experienced lithium toxicity. They had all met Research Diagnostic Criteria (13) for affective disorders, with diagnoses of bipolar disorder (N=39), unipolar depression (N=17), and schizoaffective disorder (N=29).

Except for lithium and hypnotics, none of the patients had received any psychotropic drugs for at least 1 month before testing. It was one of the principles at this research-oriented clinic that neuroleptics and antidepressants were used only during acute episodes, and the patients had not taken these drugs on a maintenance basis.

Twenty-six patients (eight men and 18 women) took lithium once daily, 42 (17 men and 25 women) twice daily, 15 three times daily, and two four times daily (five men and 12 women). In all patients, this daily regimen was maintained for a minimum of 1 year before testing. The practice on how often to give lithium has changed from frequently to less frequently because of better compliance, then back to frequently after the scare over the renal effects of lithium, and less frequently more recently (2). During these changes, some patients preferred to stay on a particular schedule. There are reasons to believe that compliance was unusually high in this group. After acceptance into the clinic all patients participated in an educational program with special emphasis on compliance. The standard monitoring schedule was once per week in the first month, once per month for the first year, and every 3 to 4 months thereafter. The serum lithium level was controlled within relatively narrow limits. Regular feedback on serum levels was provided, and issues of compliance were regularly discussed.

All patients were admitted to the hospital for kidney function testing. During this admission 24-hour urine collections were done from 4:00 p.m. one day to 4:00 p.m. the subsequent day. If the urine creatinine quantity per 24 hours was less than 8,800 μmol, the collection was repeated until adequate. Serum lithium level and serum creatinine level were determined at 9:00 a.m. during the 24-hour collection, 12 hours after the last lithium dose. On a separate day, osmolality was determined on a sample of urine collected after the patient had gone 17 hours without fluids. One hour later, after an intramuscular injection of 5 units of vasopressin in oil, the determination of urine osmolality was repeated. Creatinine clearance was determined and corrected for body surface by using height and weight.

Differences in continuous variables between the subgroups of patients taking lithium once (N=26), twice (N=42), and multiple times (three and four times) (N=17) daily were evaluated by analysis of variance (ANOVA). The difference in sex distribution was compared with the chi-square test. The difference between the groups in log urine volume was evaluated by analysis of covariance (ANCOVA), with age, sex, duration of lithium treatment, and daily dose as covariates. The effects of age, sex, duration of treatment, daily dose, and frequency of schedule as predictor variables on maximum osmolality and creatinine clearance were analyzed by multiple regression.

RESULTS

The mean values, standard deviations, and confidence intervals are presented in table 1. ANOVA showed a significant effect for duration of lithium treatment, but the trend in the means was not linear, and this finding does not refute the interpretation that we offer. ANCOVA showed a significant main effect for the daily schedule on urine volume. Post hoc analysis using Duncan's multiple range test showed a significant difference in urine volumes between subgroups

TABLE 1. (continued)

Creatinine Clearance (ml/minute)			Maximum Osmolality (mOsmol/kg)			Urine Volume^b (ml)		
Mean	SD	Confidence Interval	Mean	SD	Confidence Level	Mean^c	SD	Confidence Interval
967.5	357.7	823.0–1,112.0	761.8	170.7	692.8–830.7	1,880.0	1.5	1,621.8–2,202.9
925.4	335.2	820.9–1,029.8	676.7	220.0	608.2–745.3	1,986.1	1.6	1,710.0–2,312.1
858.4	291.5	708.4–1,008.3	664.8	169.5	577.6–752.0	2,511.9	1.6	1,967.9–3,198.9

of patients on once and multiple (three and four times) daily schedules.

Regression analysis showed that duration, daily dose, and frequency of schedule had no significant effect on maximum osmolality or creatinine clearance (data not reproduced). Age was the only significant predictor of maximum osmolality ($B=-0.30$, $p<0.05$) and creatinine clearance ($B=-0.31$, $p<0.05$).

DISCUSSION AND CONCLUSIONS

Our data are consistent with the emerging literature, which indicates that the schedule of lithium administration has a significant effect on the development of polyuria (5–8, 14). Patients who take lithium in a single daily dose given at bedtime are less likely to develop polyuria than are patients who take lithium in multiple daily doses. Patients in the present study were not randomly assigned to different daily schedules, and the conclusions are therefore only suggestive.

We could find no studies in the literature that directly contradict this conclusion; however, three reports might be interpreted as contradictory. In 1979 Hullin et al. (15) found a minimal effect of lithium on urinary volume, and they attributed these findings to lithium administration in smaller and divided daily doses (15). They acknowledged that their patients were maintained on a relatively low mean serum lithium level (0.59±0.17 mmol/liter), which might best explain the unaffected urine volumes. Donker et al. in 1979 (16) recommended that lithium be given in divided doses, as they found a lack of association between total daily dose, serum lithium level, treatment duration, and maximum osmolality. Their group, however, was relatively small, and the proportion of patients with polyuria was substantial (N=eight of 30). In 1988 Greil et al. (17) did not find a significant reduction in urine volume when they switched 15 patients from a twice-a-day schedule to a once-a-day schedule. The chance of a false negative result was high, considering the small numbers and large standard deviation.

Several authors have suggested that the benefit of a once-per-day schedule is due to a lower trough in the serum lithium level, which allows more time for renal distal tubular regeneration. The main support for this idea came from a correlation observed in one study between the minimum serum lithium level and urine volume and lack of correlation with the maximum serum level (18).

Some data in the literature are inconsistent with this simple explanation of the cause of the observed effect. Perry et al. (8) did not find that the minimum trough levels in patients on a single daily schedule were significantly lower than those of patients on multiple daily schedules; however, only eight patients were studied. It has also been reported that patients taking sustained-release lithium had better urine concentrations than patients taking regular lithium; this finding would seem to be inconsistent with the idea that a prolonged trough aids tubular regeneration and therefore reduces polyuria (10, 19). In addition, there is the lack of association between polyuria and maximum osmolality noted in some studies and evidence from our study that lithium did not affect maximum osmolality (i.e., tubular function of the kidney) but did affect urine volume (1, 11, 16).

Patients with affective disorders who have never taken lithium have often had high urine volumes on screening, and lithium may increase this even further (2, 9). Lithium has also been reported to decrease urine volume in bipolar patients with polydipsia and intermittent hyponatremia (20). These observations suggest that polyuria observed in lithium-treated patients may be due, at least in part, to extrarenal factors (9). The relationship between the thirst mechanism, antidiuretic modulation of renal water excretion, neurotransmitter disturbances in psychiatric disorders, drugs like lithium, and the well-documented partial insensitivity of the kidneys to vasopressin in patients taking lithium is likely to be complex (1, 20).

In addition to reducing the frequency of lithium administration, reduction of the total daily dose, and consequently the serum level, is also associated with a lower urine volume (1, 2, 11, 15). Since the currently accepted serum lithium levels have been developed on the multiple daily schedule, the total daily dose might have to be reduced when patients are switched to the single daily schedule, taking into account that levels might increase by 10% to 30% (1, 21). There are no definitive data at present to resolve the question of whether patients who show a higher serum lithium level after switching to a single daily schedule should be given a lower daily dose to keep the serum level in the usual range.

Our data, placed in the context of the literature, allow the conclusion that less frequent lithium administration is associated with lower urine volume. This indicates that one of the ways to prevent or manage the increase in urine volume during lithium treatment is by less frequent administration. The data also suggest that the mechanisms involved in the effects of lithium dosing schedule on urine volume might include extrarenal factors.

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Heterogeneity of Clinical Response During Placebo Treatment

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Objective: The authors attempted to identify different patterns of improvement among patients receiving placebo during clinical trials. It was hypothesized that patients who improved abruptly would differ from patients whose improvement was gradual in that they would tend to improve earlier and would tend to have less persistent improvement. Method: The subjects were 144 patients who met the DSM-III *criteria for depressive illness and were randomly assigned to placebo medication in four double-blind antidepressant drug trials. All studies lasted 6 weeks. Mood change was rated each week on a 7-point scale; a rating of 1 or 2 was considered an indication of improvement. Improvement was judged to be abrupt if the first score of 1 or 2 was immediately preceded by a score of 4 or worse, and it was classified as gradual if the first score of 1 or 2 was preceded by a score of 3 in at least 1 week. Improvement was considered persistent if a score of 1 or 2 was not followed by a score of 3 or worse in any subsequent week. Results: Of the 144 patients, 72 showed clinical improvement during at least one weekly visit; 33 improved abruptly and 39 improved gradually. The abrupt improvements occurred significantly earlier in the trial and were less likely to persist than the gradual improvements regardless of when they occurred. Conclusions: These data suggest that among patients receiving placebo abrupt improvements are a form of placebo response and gradual responses may be the result of spontaneous remission. These preliminary observations require validation.*

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Placebo effects have long been recognized (1), but neither prospective identification of placebo responders nor identification of relevant mechanisms has been achieved. Studies in nonclinical settings (2, 3) have failed to show that personality variables, demographic factors, or cognitive styles predict placebo response. Studies of psychiatric patients indicate that for patients with affective disorders, severe, chronic illness is a weak predictor of poor response during placebo treatment (4–8). In one study (9), patients with abnormal results on the dexamethasone depression test had a lower placebo response rate. Patients with disorders characterized by deterioration and infrequent remission, such as chronic schizophrenia and Alzheimer's disease, rarely exhibit any substantial placebo effects.

Research on clinical benefit during placebo treatment generally assumes a unitary process, but at least two causes are probable. Patients may improve while receiving placebo because of the natural course of the illness (spontaneous remission), or the effects may be due to the nondrug elements of treatment or setting. We use the term "placebo effect" to include all changes stemming from the nonspecific effects of a care giver and treatment setting. An inert pill may add to this process but may not be necessary.

If two processes result in a common outcome, the likelihood of understanding either is poor unless these dual pathways are identified. We have presented evidence that improvement during placebo treatment is heterogeneous (8). Depressed patients who improved during a pretreatment single-blind placebo period differed from a group that did not initially improve but did improve later during 6 weeks of double-blind placebo treatment. Those who improved during the initial

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single-blind placebo period were more mildly and more chronically depressed than those who improved during the 6-week double-blind placebo treatment.

In the study reported here, we attempted to identify different types of improvement during 6 weeks of placebo administration. We had clinically observed that some patients taking placebo improved abruptly and others gradually. The abrupt improvement was frequently dramatic; patients reported that they suddenly felt "as though a veil was lifted." Therefore, speed of improvement might be a useful means of differentiating subtypes. This would be supported if abruptness of onset was related to other outcome characteristics.

We addressed the following questions: 1) Do the times of onset of abrupt and gradual improvements differ? 2) Is it possible that all patients gradually improve with time and that this artifact explains the infrequent abrupt improvements in the later weeks of treatment? 3) Do abrupt and gradual improvements differ in persistence? 4) Do these differences support the validity of making a distinction between abrupt and gradual improvements?

METHOD

Subjects

Four clinical antidepressant trials conducted in our outpatient research clinic over 7 years constituted our data base (10–13). In these outpatient studies, all patients were between the ages of 18 and 65 years, met the *DSM-III* criteria for major depression or dysthymia, and consented to research participation. All studies lasted 6 weeks, and they included 144 patients randomly assigned to placebo medication.

The patients received placebo in a single-blind fashion for 10 days. Those who improved were removed from the study. All others were randomly assigned to drug or placebo for the next 6 weeks. Antidepressants and identical-looking placebos were given on a fixed-dose schedule. The patients were evaluated weekly and were rated, double-blind, on degree of improvement for each study week.

Measures

Change in clinical status was measured by the treating psychiatrist with the Clinical Global Impression improvement scale (CGI). This is a weekly overall rating of mood change from pretreatment baseline. Ratings are made on a 7-point scale: 1=very much improved, 2=much improved, 3=minimally improved, and 4–7=unchanged or worse. A rating of 1 or 2 was considered an indication of improvement. This is a conservative judgment connoting marked reduction of symptoms. In a clinical setting, the treatment regimen of such a patient would not be altered.

Each patient who improved was categorized as having an abrupt or gradual improvement on the basis of the first improvement. Improvements following relapses were not examined in these analyses. An improvement was judged to be abrupt if a CGI score of 1 or 2 was immediately preceded by a rating of 4 (unchanged) or worse. An improvement was defined as gradual if the week when the CGI score first reached 1 or 2 was preceded by at least 1 week of minimal improvement (CGI=3). Abrupt or gradual improvements could occur from week 1 to week 6 of the study, since the patients took placebo, single-blind, for 10 days before the 6-week double-blind phase. Patients who were minimally improved (CGI=3), unimproved (CGI=4), or worse (CGI=5–7) entered the double-blind phase. Therefore, by the end of week 1, either abrupt or gradual improvement was possible.

The definition of persistence of improvement was the same as that used in previous studies (14, 15). An improvement was considered persistent if a CGI score of 1 or 2 was not followed by a score of 3 or worse in any subsequent week of the 6-week trial. Patients whose improvement first occurred at the end of the trial (week 6) could not be evaluated for persistence and were excluded from these analyses.

Statistical Analyses

The distributions of the times of onset for the abrupt and gradual improvements were compared by means of Mann-Whitney and chi-square tests. Analysis of persistence was adjusted for differences in the amount of time following the abrupt and gradual improvements by using the Mantel-Haenszel summary chi-square test (16).

RESULTS

Of the 144 placebo patients, 50% (N=72) were rated as improved (CGI=1 or 2) for at least 1 week; 23% (33 of 144) had abrupt improvements, and 27% (39 of 144) had gradual improvements. Overall, 33% (24 of 72) of the improvements persisted.

Table 1 shows the distribution of improvements by week of occurrence. To determine if the distributions of times of onset differed between the patients with abrupt and gradual improvements, a Mann-Whitney test was performed on the entire distribution. The difference was highly significant. The proportion of abrupt improvements with placebo that occurred in the first 2 weeks was 67% (22 of 33), compared to 31% (12 of 39) of the gradual improvements.

If all patients had a tendency to improve over the 6 study weeks, by weeks 4, 5, and 6 few patients with CGI scores of 4 or more would remain. Therefore, by then abrupt improvement would be uncommon.

To test for this possible artifact, for each study week we determined the ratio of patients who had abrupt improvements to the preceding week's unimproved patients (those capable of abrupt improvement). As

TABLE 1. Timing of Onset of Abrupt and Gradual Improvement in Depressed Patients Taking Placebo[a]

	Abrupt Improvement			Gradual Improvement			Chi-Square Analysis[b]	
		Improved			Improved			
Week of Initial Improvement	Number Eligible	N	%	Number Eligible	N	%	χ^2 (df=1)	p
Early								
1	104	14	13	40	4	10	0.32	n.s.
2	82	8	10	44	8	18	1.33	n.s.
Late								
3	65	8	12	45	9	20	1.20	n.s.
4	62	2	3	31	6	19	6.34	0.009
5	54	1	2	31	7	23	9.93	0.002
6	50	0	0	27	5	19	9.90	0.002

[a] Significant overall difference between abrupt and gradual improvements (z=3.9, p=0.0001, two-tailed Mann-Whitney test corrected for ties).
[b] Proportion of patients with abrupt improvements (in relation to number eligible) versus proportion of patients with gradual improvements for each week; e.g., for week 1, 14 of 104 versus four of 40 (χ^2=0.32, df=1, n.s.).

shown in table 1, between 10% and 13% of those eligible had abrupt improvements in weeks 1 to 3, but in weeks 4 to 6 only 0% to 3% of those eligible did so.

In contrast, the proportion of patients who had gradual improvements while taking placebo, in relation to the previous week's slightly improved patients (those capable of gradual improvement), was relatively constant throughout the study; 10% in week 1 and 18%–23% thereafter. The fact that 10% could have a gradual improvement after 1 week is explained by the fact that at baseline these patients were minimally improved (compared to their status before the last 7 days of single-blind placebo administration).

To further contrast the times of onset for the abrupt and gradual improvements, each week was studied. Uncorrected chi-square tests compared the proportions of patients with abrupt and gradual improvements among the eligible patients for each of the 6 weeks (table 1). According to the Bonferroni method of correction for the increased chance of finding a significant difference with six separate tests (17), the chi-square value would have to exceed 6.9 for significance to be declared with an overall error rate of 0.05. With this conservative correction, there were statistically significant differences between the proportions of patients improving abruptly and gradually in weeks 4–6. There was clearly a tendency toward increasing differences over time: abrupt improvements with placebo were less likely to occur from week 4 on.

Table 2 shows the proportions of patients with abrupt and gradual improvements whose improvement persisted. Persistence was more common among the patients with gradual improvements than among those with abrupt improvements, and this difference increased with time. However, the abrupt improvements occurred earlier, so their lack of persistence may simply be due to the fact that these patients had more time to relapse.

Using the Mantel-Haenszel summary chi-square test, we adjusted for the different lengths of time that the patients with abrupt and gradual improvements were followed, thus taking into account the different risks for relapse. The overall proportion of improvements that were persistent differed significantly between the patients with abrupt and gradual improvements (Mantel-Haenszel χ^2=9.9, df=1, p=0.002).

TABLE 2. Persistence of Abrupt and Gradual Improvement in Depressed Patients Taking Placebo

	Abrupt Improvement			Gradual Improvement		
		Persistent Improvement			Persistent Improvement	
Week of Initial Improvement	Number Improved	N	%	Number Improved	N	%
1	14	3	21	4	2	50
2	8	1	13	8	3	38
3	8	0	0	9	4	44
4	2	0	0	6	4	67
5	1	0	0	7	5	71

DISCUSSION

Our findings suggest that two types of improvement occur with placebo. Abrupt improvements occur early and are less likely to persist. In contrast, gradual improvements occur evenly throughout the first 6 weeks of treatment and tend to persist.

Abrupt improvement may be associated with the anticipation of help, thus engendering optimism. It is therefore logical that it occurs early in treatment. Abrupt improvement during placebo treatment bears little resemblance to true response to antidepressants, which persists and occurs after a 2-week delay (14, 15). In contrast, the gradual improvements in this study of placebo resembled the true drug response, since 70% occurred after a 2-week delay and approximately 50% persisted. We attribute gradual improvement to spontaneous remission.

The dramatic onset of abrupt, transient improvement in mood suggests that some endogenous mood-elevating substance may mediate abrupt improvement. Phenylethylamine is a possible candidate, since it has been suggested that it is an endogenous amphetamine

(18). Amphetamines notoriously produce only quick, transient benefits for most depressed patients.

Although our data support the concept of different types of improvement during placebo administration, they are not conclusive. Demonstration of differences in a biochemical or psychological variable would be trenchant. Replication with a new group of patients would also be helpful. In the study described in the following paper (19), we examined data from patients receiving antidepressants to determine if the pattern of abrupt and gradual improvements in the patients taking placebo could be discerned in the hiatus before the onset of true drug benefits.

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Different Types of Placebo Response in Patients Receiving Antidepressants

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Objective: The authors studied the responses of drug-treated patients in an attempt to validate observations about abrupt and gradual improvements in patients receiving placebo. Since previous data suggested that in the first 2 weeks of antidepressant treatment specific drug effects are unlikely, the authors hypothesized that this improvement is a placebo effect. Therefore, in the first 2 weeks of antidepressant treatment abrupt and gradual improvements should have the characteristics of their placebo counterparts. Method: The subjects were 263 patients in controlled antidepressant trials lasting 6 weeks. Results: The percentage of abrupt improvements that occurred in the first 2 weeks was higher than that for gradual improvements. Abrupt improvements during the first 2 weeks of drug treatment were also less persistent than gradual improvements with drug and no more persistent than improvements with placebo during the same period. However, in weeks 3, 4, and 5, abrupt and gradual improvements with drug were equally persistent and both were more persistent than abrupt improvements with placebo. Conclusions: These data support the authors' findings about placebo. Abrupt improvements during treatment with both drug and placebo are more likely during the first 2 weeks of treatment and are less likely to persist than gradual improvements. The fact that persistence of abrupt improvements with drug in weeks 1 and 2 appears different from that of gradual improvements but appears no different after week 3 suggests that the mechanism of action of abrupt improvement with drug changes after week 2.

(Am J Psychiatry 1991; 148:197–203)

In our study described in the preceding article (1), depressed patients receiving placebo had two types of improvement: abrupt and gradual. The abrupt improvements occurred earlier and were more likely to be transient. Gradual improvement may result from spontaneous remission during placebo treatment. Abrupt improvement may stem from the optimism engendered by a care giver and therefore may be a true placebo effect. In this study, data from patients treated with antidepressants were used to validate our observations of placebo-treated patients.

Improvement during drug treatment can be due to specific drug effects, spontaneous remission, or placebo effects. We have presented data (2, 3) which suggest that in the first 2 weeks of antidepressant therapy specific drug effects are unlikely. Therefore, during this period the majority of benefit is attributable to nonspecific effects and abrupt and gradual improvements should have the characteristics of abrupt and gradual improvements with placebo. For the purpose of this paper, we will consider most improvements in weeks 1 and 2 of drug treatment to be placebo effects.

The placebo studies lasted 6 weeks, and we divided them into two periods, weeks 1 and 2 and weeks 3–5. No predictions were made about week 6 because the ratings ended then and it was not possible to assess the persistence of improvement that began in week 6. Of the abrupt improvements with placebo, 67% (22 of 33) occurred in weeks 1 and 2 and 33% (11 of 33) occurred in weeks 3–5 (1). Of the abrupt improvements in weeks 1 and 2, 82% (18 of 22) were not persistent. Of the gradual improvements with placebo, 30% (12 of 39) occurred in weeks 1 and 2 and 56% (22 of 39) were in weeks 3–5. We assumed that anti-

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depressants would not block these abrupt improvements with placebo and that they could be observed in patients receiving antidepressants.

In weeks 3–5 of placebo administration few abrupt improvements occurred. Therefore, in weeks 3–5 of antidepressant therapy abrupt improvements should be true drug effects and should be as persistent as gradual improvements.

Following are the hypotheses we made about the patterns we expected to see in the data on drug-treated patients. They involve time of onset of improvement (hypotheses 1–3), persistence of improvement (hypotheses 4–8), and interaction of time, type, and persistence of improvement (hypothesis 9).

1. The onset of abrupt nonpersistent improvement will be earlier than the onset of gradual improvement. If we focus only on nonpersistent improvements (assumed to be placebo effects), a greater proportion of abrupt improvements should mimic the improvements with placebo and occur early in the study.
2. The difference in time of onset between abrupt and gradual improvements cannot be attributed to an artifact, i.e., the absence of unimproved patients in weeks 3–5.
3. The times of onset of abrupt and gradual persistent improvements will not differ.
4. Abrupt improvements during weeks 1 and 2 will be less persistent than gradual improvements in this period.
5. Abrupt improvements in weeks 1 and 2 will be no more persistent than abrupt improvements among placebo-treated patients during the same period.
6. Abrupt improvements in weeks 3–5 will be as persistent as gradual improvements in this period, since they are more likely to be due to specific drug effects than were the improvements with placebo.
7. Since the gradual improvements in weeks 3–5 of placebo administration were probably the effects of spontaneous remission, abrupt improvements in weeks 3–5 of drug treatment will be as persistent as gradual improvements with placebo.
8. Abrupt improvements in weeks 3–5 of drug treatment will be more persistent than abrupt improvements with placebo in the same period.
9. The interaction of the following three aspects of improvement will be significant: time of onset (weeks 1 and 2 versus weeks 3–5), type (abrupt drug versus gradual drug and abrupt drug versus abrupt placebo), and persistence. Such an interaction would suggest a difference in the neurophysiologic basis of abrupt improvement with drug treatment between weeks 1 and 2 and weeks 3–5.

METHOD

Eight clinical antidepressant trials conducted by our group in an outpatient research clinic over 7 years constituted our data base (4–11). In this paper, we present data from drug-treated patients in four placebo-controlled studies (8–11), described in our earlier report (1), and from four studies that included comparisons of active drugs only (4–7). The studies were double-blind, and all of the patients were between the ages of 18 and 65 years, met the *DSM-III* criteria for major depression or dysthymia, and consented to research participation. The overwhelming majority were outpatients.

Moderately depressed patients entered placebo-controlled trials, and more severely depressed patients (Hamilton score$\geq$18) entered drug-drug trials. Each study lasted 6 weeks. The 180 patients with moderate depression were randomly assigned to active drug (mianserin, imipramine, desipramine, or phenelzine), and the 83 patients with more severe depression were treated with mianserin, amitriptyline, desipramine, tranylcypromine, or phenelzine. Other than use of different medication and lack of placebo conditions in some, the designs of these studies were equivalent. We pooled patients from several studies because large numbers of patients are required to detect patterns with relatively weak effects. This was particularly true because only the first 2 weeks of study were relevant for most observations. Any bias associated with pooling should tend to obscure, rather than enhance, patterns.

The procedures, measures, and definitions of abrupt, gradual, and persistent improvement are identical to those in the paper preceding this one (1). Each drug trial followed a 10-day single-blind placebo washout period. The patients who improved during this period were removed.

The approach to data analysis was to first contrast abrupt and gradual improvement within the more severely depressed group and the moderately depressed group. If the distributions within the two groups appeared similar, the two groups were combined and the overall abrupt and gradual improvements were compared.

The statistical tests used were similar to those used in our analyses of improvement patterns of placebo-treated patients (1). Distributions of times of onset for abrupt and gradual improvements were analyzed by means of Mann-Whitney tests. Stability of improvement (persistent versus transient) was analyzed with the Mantel-Haenszel summary chi-square test to adjust for the different lengths of time that improved patients were followed (12). To test the interaction of treatment (drug versus placebo), time of improvement (early versus late), and course of improvement (persistent versus transient), Bartlett's test for interaction was performed (13).

RESULTS

Of the moderately depressed patients, 22% (40 of 180) had abrupt improvements and 49% (89 of 180) had gradual improvements. Of the more severely depressed patients, 28% (23 of 83) had abrupt improvements and 48% (40 of 83) had gradual improvements.

In our previous study of placebo-treated patients (1),

TABLE 1. Timing of Onset of Abrupt and Gradual Improvement in Depressed Patients Taking Antidepressants Whose Improvement Did Not Persist

Group and Week of Initial Improvement	Abrupt Improvement			Gradual Improvement			Mann-Whitney Test (two-tailed)	
	Number Eligible	Improved		Number Eligible	Improved			
		N	%		N	%	z	p
More severe depression (N=83)							1.59	0.11
Early								
1	—	7	—	—	1	—		
2	—	1	—	—	2	—		
Late								
3	—	3	—	—	3	—		
4	—	2	—	—	0	—		
5	—	0	—	—	2	—		
Moderate depression (N=180)							1.94	0.05
Early								
1	—	9	—	—	4	—		
2	—	5	—	—	9	—		
Late								
3	—	4	—	—	5	—		
4	—	1	—	—	6	—		
5	—	1	—	—	1	—		
Total (N=263)							2.50	0.01
Early								
1	202	16	8	61	5	8		
2	147	6	4	89	11	12		
Late								
3	116	7	6	86	8	9		
4	70	3	4	92	6	7		
5	60	1	2	65	3	5		

23% (33 of 144) had abrupt improvements and 27% (39 of 144) had gradual improvements. Thus, there was no significant difference between the two drug groups and the placebo group in the proportion of abrupt responders: 22%, 28%, and 23%, respectively (χ^2=1.1, df=2, n.s.). The proportions of gradual improvements in the two drug groups were also similar (49% and 48%), and both were significantly greater than the proportion of gradual improvements with placebo (27%), both overall (χ^2=18.5, df=2, p=0.001) and in comparisons of placebo versus drug in the moderately depressed patients (χ^2=15.8, df=1, p=0.001) and of placebo versus drug in the patients with more severe depression (χ^2=9.4, df=1, p=0.002).

Time of Onset of Improvement

Nonpersistent improvement. The time of onset of nonpersistent improvement differed between the abrupt and gradual improvements. Table 1 shows the distribution of nonpersistent improvements by week of occurrence. For the patients with more severe depression, 62% (eight of 13) of the abrupt improvements but 38% (three of eight) of the gradual improvements occurred in the first 2 weeks. In the moderately depressed group, 70% (14 of 20) of the abrupt improvements but 44% (11 of 25) of the gradual improvements occurred in the first 2 weeks. For all the patients who experienced nonpersistent improvement, 67% (22 of 33) of the abrupt improvements but only 48% (16 of 33) of the gradual improvements occurred in the first 2 weeks. Thus, the relationship between the times of onset of nonpersistent abrupt and gradual improvements with drug appears to be similar to that for placebo in that abrupt improvements occur earlier in the 6-week period.

If all patients tended to improve over time, few unimproved patients would remain in weeks 4 and 5 and by definition abrupt improvement would be uncommon. Therefore, the difference in time of onset between the abrupt and gradual improvements might be an artifact. We hypothesized that this was not the case and, for each study week, compared the number of abrupt and gradual improvements to the number of patients eligible for such improvements. As shown in table 1, for the total group of patients with nonpersistent improvement, in week 1 the percentages of abrupt and gradual improvements were equal (8%). Thereafter, the percentages for abrupt improvement diminished consistently. Only in week 1 were the percentages of abrupt and gradual improvements equal, in spite of the fact that from week 3 on 60–116 patients were unimproved and capable of abrupt improvement. Therefore, the difference in distribution found with the Mann-Whitney test does not appear to be an artifact of group improvement over time. This is essentially what was found with placebo: only in week 1 was the percentage of abrupt improvements with placebo greater than the percentage of gradual improvements (1).

Persistent improvement. In the more severely depressed group, 25% (two of eight) of the abrupt improvements and 26% (seven of 27) of the gradual improvements occurred in the first 2 weeks (table 2). In the moderately depressed group, 18% (three of 17) of

TABLE 2. Timing of Onset of Abrupt and Gradual Improvement in Depressed Patients Taking Antidepressants Whose Improvement Persisted

Group and Week of Initial Improvement	Abrupt Improvement			Gradual Improvement			Mann-Whitney Test (two-tailed)	
	Number Eligible	Improved N	Improved %	Number Eligible	Improved N	Improved %	z	p
More severe depression (N=83)							0.16	n.s.
Early								
1	—	0	—	—	1	—		
2	—	2	—	—	6	—		
Late								
3	—	3	—	—	9	—		
4	—	1	—	—	7	—		
5	—	2	—	—	4	—		
Moderate depression (N=180)							0.49	n.s.
Early								
1	—	2	—	—	3	—		
2	—	1	—	—	8	—		
Late								
3	—	5	—	—	8	—		
4	—	5	—	—	15	—		
5	—	4	—	—	15	—		
Total (N=263)							0.20	n.s.
Early								
1	202	2	1	61	4	7		
2	147	3	2	89	14	16		
Late								
3	116	8	7	86	17	20		
4	70	6	9	92	22	24		
5	60	6	10	65	19	29		

the abrupt improvements and 22% (11 of 49) of the gradual improvements occurred in the first 2 weeks. Mann-Whitney tests indicated that the differences between the times of onset of the abrupt and gradual improvements were not significant.

In the total group of patients with persistent improvement, in every week the proportion of abrupt improvements, in relation to the number of patients eligible, was less than the proportion of gradual improvements (table 2).

Overall findings. The only week in which the proportion of abrupt improvements was equal to the proportion of gradual improvements was week 1, and this was true only for nonpersistent improvement. The relationship between the times of onset for abrupt and gradual improvements with placebo (1) also appears to characterize abrupt and gradual nonpersistent improvements with drug. This is consistent with the hypotheses that these improvements during drug treatment are placebo responses and that the mechanisms responsible for them are similar to those for improvements during placebo treatment.

Persistence of Improvement

An improvement was defined as persistent if it was not followed by relapse during the period of observation. Table 3 shows the numbers of persistent abrupt and gradual improvements by week of onset. Among the total group of patients, the greatest differences between abrupt and gradual improvements in the percentage that were persistent were in weeks 1 and 2 (week 1, 11% and 44%, respectively; week 2, 33% and 56%), which is consistent with the hypothesis that abrupt improvements in weeks 1 and 2 are nonpersistent placebo responses.

However, the abrupt improvements tended to occur early in the study (18 abrupt versus nine gradual improvements in week 1), whereas the gradual improvements tended to occur more uniformly over time. Since the abrupt improvements tended to occur early, these patients had a greater opportunity to relapse before the end of the study. To control for this possible confounding effect, the Mantel-Haenszel summary chi-square test was done. This test adjusts for the different risks of relapse attributable to the different lengths of time the groups with abrupt and gradual improvements were observed. The Mantel-Haenszel test was done for each period (weeks 1 and 2, weeks 3–5, and weeks 1–5) and for the moderately and more severely depressed patients separately and combined. The results are summarized in table 3. Within each time period for each group, there was some fluctuation in outcome because of the small numbers of subjects. We therefore focus attention on the results with the total group. For weeks 1 and 2 the difference was significant, suggesting abrupt improvement early in drug treatment is less persistent than gradual improvement.

The persistence of the abrupt improvements in weeks 1 and 2 among the total group of patients receiving drug was contrasted with that for the patients receiving placebo (1). No difference was found in the proportions of persistent improvement (Mantel-Haenszel $\chi^2=0.0$, df=1, n.s.).

TABLE 3. Persistence of Abrupt and Gradual Improvement in Depressed Patients Taking Antidepressants

Group and Week of Initial Improvement	Abrupt Improvement			Gradual Improvement			Mantel-Haenszel Summary Chi-Square Test	
	Number Improved	Persistent Improvement		Number Improved	Persistent Improvement			
		N	%		N	%	χ^2 (df=1)	p
More severe depression								
Weeks 1 and 2							1.4	n.s.
1	7	0	0	2	1	50		
2	3	2	67	8	6	75		
Weeks 3–5							2.2	n.s.
3	6	3	50	12	9	75		
4	3	1	33	7	7	100		
5	2	2	100	6	4	67		
Weeks 1–5							3.5	0.06
Moderate depression								
Weeks 1 and 2							2.9	0.09
1	11	2	18	7	3	43		
2	6	1	17	17	8	47		
Weeks 3–5							0.0	n.s.
3	9	5	56	13	8	62		
4	6	5	83	21	15	71		
5	5	4	80	16	15	94		
Weeks 1–5							1.5	n.s.
Total								
Weeks 1 and 2							4.4	0.04
1	18	2	11	9	4	44		
2	9	3	33	25	14	56		
Weeks 3–5							1.2	n.s.
3	15	8	53	25	17	68		
4	9	6	67	28	22	79		
5	7	6	86	22	19	86		
Weeks 1–5							4.7	0.03

We had predicted that the abrupt and gradual improvements during weeks 3–5 of drug treatment would be equally persistent. The Mantel-Haenszel test indicated that the proportions of persistent improvement for weeks 3–5 were not significantly different.

A Mantel-Haenszel test also showed no significant difference between the proportion of gradual improvements during weeks 3–5 of placebo administration that were persistent (1) and the proportion of persistent abrupt improvements with drug during the same period ($\chi^2=0.36$, df=1, n.s.).

We had also hypothesized that abrupt improvements during weeks 3–5 of drug treatment would be more persistent than abrupt improvements with placebo in the same period. The proportions of abrupt improvements in weeks 3–5 that were persistent were 65% (20 of 31) for drug and 0% (none of 11) for placebo, which were significantly different according to a Mantel-Haenszel test ($\chi^2=9.44$, df=1, p=0.002), even when the differences in time of onset were corrected for.

Difference in Mechanism of Abrupt Improvement Between Weeks 1 and 2 and Weeks 3–5

We predicted a significant interaction among time of response (weeks 1 and 2 versus weeks 3–5), type of improvement (abrupt drug versus gradual drug and abrupt drug versus abrupt placebo), and the proportion of persistent improvements. Bartlett's test was used to contrast the difference between the proportions of abrupt and gradual persistent improvements with drug in weeks 1 and 2 with the corresponding difference for weeks 3–5. The persistence of the gradual and abrupt improvements in the severely depressed, moderately depressed, and total patient groups is shown in table 4. All differences were in the same direction, so to simplify the presentation we will discuss only the comparisons for the total group. In weeks 1 and 2, the difference in persistence between abrupt improvement (19%) and gradual improvement (53%) was 34%. In weeks 3–5, there was a 12% difference (65% and 77%, respectively). The relatively large difference in weeks 1 and 2 and the relatively small difference in weeks 3–5 were as expected, but the interaction was not significant ($\chi^2=1.6$, df=1, p=0.2).

We also contrasted the data on persistence for the total group of patients with those for the placebo-treated patients previously studied (table 4). There was a significant interaction between abrupt improvements with drug and abrupt improvements with placebo. This finding is attributable to the low percentages of persistence (19% and 13%, respectively) for both groups (drug and placebo) in weeks 1 and 2. In weeks 3–5, 65% of the abrupt improvements with drug and 0% of the abrupt improvements with placebo were persistent. This finding is consistent with the hypothesis that only in weeks 1 and 2 are abrupt improve-

TABLE 4. Interaction Among Time of Onset, Type, and Persistence of Improvement in Depressed Patients Taking Antidepressants or Placebo[a]

	Onset of Improvement in Weeks 1 and 2			Onset of Improvement in Weeks 3–5		
		Persistent Improvement			Persistent Improvement	
Speed of Improvement and Group	Number Improved	N	%	Number Improved	N	%
Abrupt improvement						
Drug	27	5	19	31	20	65
More severe depression	10	2	20	11	6	55
Moderate depression	17	3	18	20	14	70
Placebo	22	4	18	11	0	0
Gradual improvement						
Drug	34	18	53	75	58	77
More severe depression	10	7	70	25	20	80
Moderate depression	24	11	46	50	38	75
Placebo	12	5	42	22	13	59

[a] The data on patients receiving placebo are from the study reported in the preceding article (1). The interaction between abrupt improvements in the total group of drug-treated patients and in the placebo-treated patients was significant ($\chi^2=8.7$, df=1, p=0.003, Bartlett's test).

ments with drug and placebo similar and that the abrupt improvements in weeks 3–5 differ. When the data from the severely and moderately depressed patients given drug were separately compared with the data from the placebo-treated patients, there were virtually identical interactions (these data are available on request).

When the gradual improvements with placebo and drug were contrasted, there was little evidence of an interaction ($\chi^2=0.2$, df=1, n.s.); for weeks 1 and 2 the difference in persistence between the drug and placebo groups was 11%, and for weeks 3–5 the difference was 18% (table 4). This is consistent with the interpretation that the same mechanism is responsible for gradual improvement in both the early and later weeks of drug treatment.

DISCUSSION

The results of our previous study (1) suggested there are two types of improvements during placebo administration. The abrupt improvement occurs early and has a low likelihood of persisting. In contrast, gradual improvements with placebo are evenly distributed over the first 6 weeks of treatment and tend to persist.

To what extent are these observations validated by the responses of patients receiving drug? Many factors contribute to change in clinical status among patients taking antidepressants, including hope, true drug response, and nonspecific therapeutic effects. In some patients, side effects may obscure beneficial effects.

In spite of such obfuscating factors, in weeks 1 and 2 of the trials we examined, the abrupt improvements of drug-treated patients appeared indistinguishable from the abrupt improvements of patients receiving placebo. Few of them persisted. This analysis serves as an independent replication of our observation of abrupt improvement with placebo. The data are consistent with the hypothesis that the same neurophysiologic process is responsible for early abrupt improvements during drug and placebo treatment. Abrupt improvements with drug and placebo that occur later than 2 weeks appear to be different. This finding coincides with the hypothesized time of onset of true antidepressant effects (2, 3).

Thus, there appear to be two types of abrupt improvements during drug treatment: an early placebo effect and a later specific drug response. Gradual improvements during drug treatment presumably include both spontaneous remissions and true drug responses. In our study there was little difference between the gradual improvements with drug and placebo either early or late in treatment, so it is impossible to determine which gradual improvements during drug treatment were due to spontaneous remission. However, there were about twice as many gradual improvements with drug (49%, 129 of 263) as with placebo (27%, 39 of 144).

Our findings therefore suggest several routes to improvement during drug treatment. Patients who abruptly improve early in treatment probably improve as a result of a placebo effect; late abrupt and gradual improvements appear to be persistent, true drug effects. Although gradual improvements due to spontaneous remission must occur during drug treatment, we were unable to individually identify them.

This work has implications for the clinician. We selected 2 weeks as the point to divide the study into phases. Although empirically derived from prior work, this cutoff is somewhat arbitrary. Depending on dose, rate of absorption of drug, diagnosis, and other variables, the onset of true antidepressant effect might be slightly earlier or later than 2 weeks. The important point is that abrupt improvement early in drug treatment has a good chance of being a placebo effect and of being followed by relapse. Abrupt improvement was observed in both the severely and moderately depressed patients receiving drug. Patients with this type of response should be observed closely over time because relapse is likely. If such patients relapse, it might not mean that they have ceased to experience a true drug effect and that antidepressants are not a useful treatment for them. Rather, it may mean that improvement with the first drug was nonspecific and that another antidepressant should be tried. This may also apply to sudden improvement with psychotherapy. Such patients should be observed more closely for relapse.

In summary, the validity of our previous observations about abrupt improvement during placebo administration (1) was enhanced by the data from drug-treated patients. Researchers studying placebo effects should consider these observations, which may be applicable to other areas. Our findings should encourage separate examination of the different types of improvement in studies of the biochemical basis of improvement during drug or placebo administration.

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A National Study of Psychiatric Hospital Care

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Background: *The delivery system for psychiatric inpatient services in the United States has changed dramatically over the past 30 years, undergoing a marked privatization.* *Method:* *To assess the effect of changes in ownership and types of inpatient settings on the structure of the mental health services system, the authors surveyed a national sample of nonfederal mental health facilities in 1988.* *Results:* *Comparing their data to those of earlier surveys, they found that a decline in the number of patients per staff occurred in most settings over the last decade, suggesting that this aspect of quality of care may have improved. They observed important ownership-related differences in 1988 in diagnostic mix (e.g., more schizophrenia treated in public facilities than in private ones) and in payer source (e.g., more third-party revenues in public facilities than occurred in the past).* *Conclusions:* *There was a significant interaction between ownership form and type of facility, suggesting that the type of inpatient setting, ownership, and the relation between the two should be considered in assessing the impact of privatization on the accessibility of health care available for the mentally ill. The authors found that the increase in private psychiatric hospitals has widened the availability and choice of treatment facilities for those with private funding sources (especially children and adolescents) but has not had a similar effect in increasing sources of care for the seriously mentally ill dependent upon public financing.*

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The system of hospital care in the United States has evolved and changed dramatically in the twentieth century, and one important dimension of change has been increasing privatization and corporatization (1, 2). The trends toward for-profit ownership and emphasis on the business aspects of health care have also recently influenced the development of psychiatric hospital services (3, 4). The growth of private hospital services has not only changed the mix of ownership of inpatient mental health care providers, but it may potentially influence access to and the nature of mental health care. Several previous studies have described the trends in the numbers of facilities and of patients. The current study examined, through a national survey of inpatient mental health facilities, the trends and differences in patient care in hospitals as a function of ownership (public versus private) and type (general versus specialty). This paper summarizes findings with respect to diagnostic mix, source of payment, staffing patterns, and selected aspects of quality assurance and community services.

The economist Burton Weisbrod (5) noted that different ownership forms—proprietary, public, and nonprofit—typically have characteristic missions and goals. Using legal ownership as a proxy for mission, our study suggests that some of these differences apply to psychiatric hospitals. The initial focus of the current study was to examine the relationship between ownership form and a variety of measures related to access to and provision of care, such as service mix, diagnostic mix, payer mix, staffing patterns, quality assurance monitoring, and so forth.

The overall aim of the study was to examine the relationship between the ownership of hospitals and the extent of 1) access to care, 2) continuity of care for patients, and 3) the configuration of the hospital mental health care system. We anticipated that these dimensions of hospital care would be affected by ownership in several ways. First, the ownership form (for-profit, private nonprofit, or public) of the individual hospital creates incentives that alter the behavior of the institution. Second, the type of facility (specialty or

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general hospital) would influence access to services. Third, competition from for-profit hospitals may influence the behavior of private nonprofit and public institutions in the same local service area.

In general, we expected that there would be differences, related to the ownership form of the hospital, in the patient and service mix. For example, on the basis of previous studies, we expected that private hospitals and general hospitals would tend to treat fewer chronic patients and that they would favor patients with private insurance. The current study describes the effect of ownership form and of hospital type separately and in combination. For purposes of the analysis, we have used six categories of ownership type: public specialty, private nonprofit specialty, private for-profit specialty, public general, private nonprofit general, and private for-profit general.

It is estimated that for over two decades roughly 14% of the total health care expenditures in the United States have been for alcohol, drug abuse, and mental disorders; however, during this time the system of inpatient mental health care in the United States has undergone major structural changes (6). Today there are fewer than one-third as many psychiatric beds as there were 30 years ago; admission rates per 100,000 population to public mental hospitals are now the lowest in the past 100 years (7). Whereas 20 years ago 95% of these beds were in the public sector, today less than 50% are government owned. Although estimates vary, we estimate that the number of private psychiatric hospitals has burgeoned over the past decade, growing from 184 in 1979 to more than 450 in 1990 (8). There has been a corresponding shift to for-profit ownership, with proprietary psychiatric hospitals—largely free-standing specialty facilities—growing from 88 in 1979 to 350 in 1988 (9). Of these, 90% are operated under the auspices of investor-owned, multihospital systems and over 75% are located in 15 states, primarily in the South and West (4). A coinciding change has been the growth in the number of psychiatric units (largely nonprofit) in general hospitals to roughly 1,500 in 1989, double the number 20 years earlier (9). As a result, private psychiatric beds are currently divided equally between specialty (primarily for-profit) and general (primarily nonprofit) hospitals. There are reasons to expect that each of these changes may significantly alter the nature of mental health care in the United States (2). Studies of general health care providers have found that, compared to public hospitals, private nonprofit and particularly for-profit facilities are more likely to restrict access to care by uninsured patients (10–12).

The extent to which newly emerging nonprofit and for-profit psychiatric hospitals will differ from their older public counterparts will depend on several mediating factors. These include the strength of ties between the hospital and community (and therefore administrators' sense of a fiduciary responsibility to the community) and the extent of competition among health care providers based on the prices they charge for services. Facilities with a strong sense of community responsibility will likely develop services that have significant community benefits, even if unprofitable, in this way emulating the public orientation of government-operated mental health care facilities (13, 14). Historically, private nonprofit hospitals have more often espoused a community orientation than have their for-profit counterparts, in part because their boards of directors tend to be more representative of the community (15, 16). This relationship typically developed over many years and was particularly strong in those facilities founded before World War II, a period in which health care institutions depended heavily on philanthropy from the community to support their operating and capital costs (12, 17, 18). Newly constructed psychiatric hospitals, largely for-profit, may lack these well-established community ties. Psychiatric units established in older community hospitals may or may not emulate the values or mission of the host institution (3, 19).

THE NATIONAL MENTAL HEALTH FACILITIES STUDY

The National Mental Health Facilities Study, conducted by the Center for Social Policy of the John F. Kennedy School of Government, Harvard University, and funded by the National Institute of Mental Health (NIMH), was designed to address these unanswered questions about the ongoing privatization of mental health services in the United States. The survey consisted of a 200-item questionnaire (with telephone follow-up for missing information) mailed to administrators of all nonfederal psychiatric hospitals in the United States, including community mental health centers with inpatient units, and a 75% random sample of psychiatric units in nonfederal general hospitals. The sample was cross-checked with listings from the NIMH Master Facility File, the American Hospital Association (AHA), and the National Association of Private Psychiatric Hospitals (NAPPH). A total of 1,500 hospitals were surveyed in 1988, and responses were received from 915 hospitals, a 60% response rate, although the rate varied from 78% for public specialty to 38% for for-profit specialty hospitals. This overall rate is comparable to that achieved by similar surveys. We received completed surveys from 173 state and county mental hospitals, 176 private psychiatric hospitals, and 566 psychiatric units in general hospitals. Of the private psychiatric hospitals, 112 were for-profit and 64 were nonprofit. Of the general hospitals, 413 were nonprofit, 37 were for-profit, and 116 were public. Data were collected between October 1987 and May 1988.

Specific questions were drawn from survey instruments used by NIMH, AHA, NAPPH, and numerous survey researchers. Following revisions by a national

TABLE 1. Diagnoses of Patients Admitted to Nonfederal U.S. Psychiatric Hospitals and Units in 1988[a]

	Percent of Patients[b]													
	Specialty Hospital						General Hospital Unit							
	Public (N=172)[c]		Nonprofit (N=63)		For-Profit (N=106)[c]		Public (N=115)[c]		Nonprofit (N=411)[c]		For-Profit (N=36)		ANOVA	
Diagnosis	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F	df
Schizophrenia	44.2_a	16.7	$21.5_{b,c}$	16.0	18.1_c	20.3	29.4_d	17.9	23.5_b	15.6	$21.7_{b,c,d}$	14.7	48.37[d]	5, 896
Depression	18.2_a	10.0	$34.0_{b,d}$	18.5	34.7_d	21.0	27.2_b	14.7	35.2_d	18.9	$26.7_{a,b,d}$	20.0	26.20[d]	5, 898
Substance abuse	$13.1_{a,d}$	15.0	$13.1_{a,d}$	13.4	16.8_a	19.5	$13.8_{a,d}$	14.6	10.5_d	13.5	$15.9_{a,d}$	14.7	3.96[e]	5, 898
Disorders of childhood and adolescence	4.4_a	6.3	10.0_d	13.5	15.6_b	17.6	5.1_a	6.4	5.1_a	9.4	$8.0_{a,d}$	10.1	21.76[d]	5, 897
Other[f]	20.2_a	12.7	$21.6_{a,d}$	13.5	14.6_c	11.4	$24.3_{a,d}$	12.8	25.9_d	14.9	28.0_d	22.0	20.67[d]	5, 891

[a] Data are unweighted with respect to number of patients represented by each reporting institution.

[b] Matching subscripts indicate nonsignificant differences. Means in same row that do not share a subscript differ at $p \leq 0.05$ (Tukey's Studentized range test).

[c] Numbers vary slightly for each analysis.

[d] $p \leq 0.0001$.

[e] $p \leq 0.002$.

[f] For example, personality disorders, anxiety disorders, and organic brain syndrome.

advisory panel, a nationwide pretest was conducted in the summer of 1987. The final instrument was distributed, and the resulting 915 responses were analyzed by using the Statistical Analysis System General Linear Models procedure for analysis of variance in order to accommodate unequal cell sizes. The overall statistical analyses employed the independent variable Owntype. Comparisons of individual means used Tukey's studentized range test.

To try to avoid the possibility of nonresponse bias, we took several steps to counteract this possibility for our survey. The lowest response rate for hospitals in our sample was for for-profit specialty facilities (38%). In our pretest, we discovered that the reason for nonresponse of many of these facilities was a heightened concern with the pressures of competition felt by these hospitals or their parent organizations. Despite assurances of anonymity, respondents expressed fears that data about their individual hospital or about a particular firm would be identified, to the detriment of their competitive position or their image. Still, we received 112 usable responses distributed throughout the country and between corporate-owned and independent hospitals. As an additional check on the possibility of sample bias, we compared our findings for this category of hospitals on the variables reported here (diagnoses, sources of revenue, and staffing) with data from surveys by NIMH (1986) and NAPPH (1988). We found the results, where comparable, to be quite consistent, suggesting only a small risk in generalizing from data about our sample to the population of all such hospitals. For example, the NAPPH survey of private specialty hospitals reported an average of 106 beds per facility, compared to 108 for these hospitals in the current sample. The average occupancy rate reported by NAPPH was 68%, compared to 69% in our sample. Measures of diagnostic mix and revenue source were also similar in the two samples.

OWNERSHIP, CONTROL, AND HOSPITAL PERFORMANCE

Access to Care

Previous studies of psychiatric hospitals have found that patients were selected for admission to private hospitals partly on the basis of ability to pay, but it was unclear whether, within ownership categories, specialty and general hospitals treated patients with different psychiatric conditions (14, 20, 21). Nor was it clear whether psychiatric units of general hospitals would follow the same ownership-related patterns in admitting patients as did psychiatric specialty hospitals.

Diagnostic mix. Table 1 presents the 1988 diagnostic mix of inpatients in surveyed hospitals, according to ownership and type of facility. Several patterns emerge. Public hospitals—especially specialty hospitals—are more likely to treat patients with schizophrenia than are private ones (F=168.03, df=1, 900, p=0.0001). Among specialty hospitals, those privately owned treated twice as high a proportion of patients with a diagnosis of depression. Schizophrenia is usually a psychiatric disorder with onset early in life, one that is commonly chronic and recurrent and is often associated with marked disability of psychosocial functioning (22). These patients are costlier if for no other reason than that they have a considerably—two to three times—longer average length of stay (at least in public facilities) than do patients with an affective disorder or chemical dependency (6, 20). These case mix differences thus suggest that private facilities are specializing in disorders that usually respond to short-term treatment. For schizophrenia and depression, the mix of patients in inpatient psychiatric units of general hospitals, whatever their ownership, looks more like that of private than public psychiatric hospitals. This undoubtedly reflects a focus in these units on patients who will respond to short-term treatment, although it is

TABLE 2. Source of Revenues for Nonfederal U.S. Psychiatric Hospitals and Units in 1988

Source of Revenue	Percent of Revenue[a]												ANOVA	
	Specialty Hospital						General Hospital Unit							
	Public (N=159)[b]		Nonprofit (N=64)		For-Profit (N=109)[b]		Public (N=113)[b]		Nonprofit (N=406)[b]		For-Profit (N=35)[b]			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F	df
Insurance[c]	13.3_a	15.8	53.8_b	27.4	68.3_c	26.7	32.4_d	22.8	43.1_e	18.1	$48.7_{b,e}$	15.4	108.30[d]	5, 875
Medicare	17.9_a	18.8	$13.5_{a,b}$	10.9	11.1_b	12.3	$19.8_{a,c}$	12.0	25.7_d	12.9	$27.2_{c,d}$	13.4	27.44[d]	5, 882
Medicaid	22.7_a	23.3	10.0_b	16.8	9.6_b	21.9	24.6_a	19.9	20.0_a	14.5	$16.2_{a,b}$	16.9	12.72[d]	5, 882
State government and contracts	35.1_a	40.6	13.0_b	24.5	$3.6_{c,d}$	9.9	$11.2_{b,c}$	21.5	2.8_d	6.9	$2.0_{b,c,d}$	4.7	59.42[d]	5, 880
Patient and other	$9.6_{a,c}$	14.0	$7.0_{a,b}$	8.0	5.5_b	6.7	11.5_c	12.6	$8.0_{a,b}$	7.7	$6.6_{a,b,c}$	7.3	5.22[d]	5, 879

[a] Matching subscripts indicate nonsignificant differences. Means in same row that do not share a subscript differ at $p \le 0.05$ (Tukey's Studentized range test).

[b] Numbers vary slightly for each analysis.

[c] Blue Cross/Blue Shield, commercial insurance, and health maintenance organizations.

[d] $p \le 0.0001$.

notable that about a quarter of the patient population in these units has a primary diagnosis of schizophrenia.

Specialty hospitals admit a greater proportion of patients for treatment of disorders of childhood and adolescence than do general hospitals (F=24.93, df=1, 901, p=0.0001). Among specialty facilities, for-profit hospitals treat the largest proportion of these patients, followed by private nonprofit facilities. Public specialty hospitals treat the smallest proportion (F=21.76, df=5, 897, p=0.0001). These types of disorders have long been characterized by unmet need for inpatient care, suggesting that an influx of private capital may be filling an important gap. It is also worth noting, however, that there have been concerns about excessive hospitalization, in lieu of outpatient care (21, 23).

Source of revenue. The data in table 2 on source of revenues by ownership and type of facility are important for several reasons. First, the intermixing of public with private financing in both public and private facilities is the main statistical effect. Although public specialty psychiatric hospitals are often perceived by policy makers to be financed by the states apart from mainstream health insurance, in fact over half their revenues come from third-party payers such as Medicare, Medicaid, and commercial insurers. This is even more true for public general hospitals, which obtain over three-quarters of their revenues from third-party sources. We postulate that, funded in this manner, the government-operated system of psychiatric hospitals may be subject to many of the same reimbursement-induced influences as are their private counterparts. Conversely, private hospitals receive a significant proportion of their funding from public sources, despite restrictions and biases against Medicaid payments for adult patients ages 21–64 in specialty psychiatric facilities (11). Also, among private nonprofit psychiatric (specialty) hospitals and general hospital psychiatric units, over one-third of all revenues come from public auspices under either state grants or Medicaid and Medicare. For-profit hospitals receive one-quarter of their revenues from these sources. Comparison of payer source as a function of both ownership and type of facility is presented in table 2.

Private insurance paid for more than 40% of psychiatric patient care overall and more than two-thirds of revenues in for-profit specialty hospitals. Blue Cross/Blue Shield, the largest private insurer in many states, paid for 15% of revenues overall (not shown separately in table 2). Health maintenance organizations (HMOs) and preferred provider organizations (not shown separately) account for a relatively small proportion of revenues: 5% in nonprofit facilities (7% in nonprofit specialty facilities) and less than 1% in public ones. Since HMOs enrolled one-tenth of the American population at the time, these numbers are strikingly low. They suggest that HMOs may be unusually effective at avoiding hospitalization, may enroll an atypically healthy population, or may significantly restrict access to mental health care (24–27).

Quality of Care

In the absence of reliable outcome measures, indirect indicators must serve to measure quality in mental health care (28). To this end, we collected information on staffing patterns and policies concerning aftercare. Although there may not always be an unambiguous link between these measures and health outcomes, we believe that they offer some useful insights into determining quality of inpatient treatment.

Staffing ratios. The number of patients per full-time equivalent staff (patient-staff ratios) reported on the survey is shown by ownership and type of facility in table 3. We distinguish here between psychiatrists employed by the hospital and those in private practice who provide inpatient care only for patients they have admitted. The 1988 data collected in this survey were also compared with data collected in earlier NIMH surveys. When we made adjustments for differences in data collection methods, we found that, over the past 10 years, there have been significant decreases in the

TABLE 3. Ratio of Patients to Full-Time Staff in Nonfederal U.S. Psychiatric Hospitals and Units in 1988

	Specialty Hospital									General Hospital Unit										
	Public			Nonprofit			For-Profit			Public			Nonprofit			For-Profit				
		Ratio^{a,b}			Ratio^{a,b}			Ratio^{a,b}			Ratio^{a,b}			Ratio^{a,b}			Ratio^{a,b}		ANOVA	
Staff	N^a	Mean	SD	N^a	Mean	SD	N^a	Mean	SD	N^a	Mean	SD	N^a	Mean	SD	N^a	Mean	SD	F	df
All psychiatrists	167	31.7_a	32.6	64	12.8_b	17.2	111	18.5_b	29.2	113	11.1_c	11.2	405	9.3_c	8.0	35	$13.1_{b,c}$	16.7	33.29^c	5, 839
Staff psychiatrists	165	32.0_a	32.6	52	21.6_c	26.7	77	31.6_c	29.0	71	10.1_b	11.0	235	15.5_b	14.1	13	16.0_c	14.2	16.07^c	5, 607
Private attending psychiatrists	—	—	—	43	$29.3_{a,b}$	32.7	93	33.1_a	48.4	62	$17.8_{b,c}$	15.7	360	15.9_c	19.6	32	$14.8_{b,c}$	17.2	9.31^c	5, 535
Psychologists	160	68.5_a	75.6	53	26.2_c	35.7	70	43.3_b	37.7	63	15.6_c	13.6	203	19.3_c	16.2	14	17.3_c	8.5	25.99^c	5, 557
Social workers	170	29.6_a	30.1	60	10.8_b	11.4	105	16.7_b	17.6	107	12.1_b	20.6	383	12.7_b	9.6	34	17.1_b	12.6	23.67^c	5, 853
Registered nurses	170	5.8_a	6.0	63	3.0_d	4.9	109	3.8_b	4.8	111	1.8_c	1.6	404	1.7_c	1.7	35	2.3_d	3.3	34.47^c	5, 836
L.P.N., mental health worker, other direct care provider	155	1.5_a	1.5	45	$1.5_{a,b}$	1.5	91	1.5_b	0.8	77	$1.6_{a,b}$	1.1	246	2.1_b	1.8	29	$2.0_{a,b}$	1.0	4.44^d	5, 637

[a] Based on responses greater than zero.

[b] Matching subscripts indicate nonsignificant differences. Means in same row that do not share a subscript differ at $p \leq 0.05$ (Tukey's Studentized range test).

[c] $p \leq 0.0001$.

[d] $p \leq 0.0005$.

ratio of patients to professional staff in inpatient units both in public and private facilities. These changes have been greatest in facilities that previously had the least adequate staffing (e.g., state and county hospitals), leading to a convergence on this measure of quality of care over time across different types of ownership. Nonprofit facilities also still have lower patient-staff ratios than do public or for-profit facilities in most, but not all, categories of professional staffing, e.g., psychiatrists, psychologists, social workers, and registered nurses (29). Overall, public psychiatric hospitals have relatively fewer professional personnel. Detailed comparisons are difficult because of different methods of enumerating staff.

Interestingly, the staffing patterns in public general hospital units resemble nonprofit, and to some extent for-profit, specialty facilities more than they do public specialty facilities. They also have proportionately more trainees than any other category of facility (not shown in table 3): 40% of public general hospitals, 34% of nonprofit specialty hospitals, and 27% of public specialty hospitals were affiliated with accredited residency training programs, compared with 6% of for-profit hospitals (both types).

Staffing patterns reveal several additional ownership-related main effects. The first involves the relative emphasis on medical practitioners (psychiatrists and registered nurses) or what is commonly referred to as the medical model. Not surprisingly, the medical model is most prevalent in the psychiatric units of general hospitals, as reflected in the relatively low patient-staff ratios for psychiatrists (F=35.15, df=1, 824, p=0.0001) and registered nurses (F=130.32, df=1, 890, p=0.0001), compared to specialty hospitals. For-profit psychiatric hospitals follow a similar pattern, while their public and private nonprofit counterparts place a greater emphasis on nonmedical providers.

In general, for-profit facilities rely less on nonmedical professionals than do nonprofit facilities. Psychologists are poorly represented, particularly in specialty for-profit hospitals, where the ratio of psychiatrists to psychologists is 2 to 1. In for-profit specialty facilities, psychiatrists and psychologists are comparably represented among the employed staff, but when private attending staff are included, psychiatrists are better represented by a factor of 2.

Monitoring treatment. Regulators and payers increasingly examine patterns of practice in psychiatry and other areas of medicine to determine behaviors that improve both quality of care and cost effectiveness: patient care activities in hospitals are subjected to peer review and utilization review by independent outside agents (30). Insurance company requirements dictate not only prior approval for admission but also lengths of stay, appropriate procedures and tests, and comparison of practices to statistical norms for the hospital or the region (31). And there is growing emphasis on quality of care measures by the Joint Commission on Accreditation of Health Organizations. How well these procedural methods of quality assurance actually correlate with quality of care is still unclear. Nonetheless, these activities are often used as measures of the practice patterns in hospitals. An especially important dimension of treatment is aftercare.

Monitoring aftercare. Good quality mental health care requires a successful transition from care as an inpatient to living in the community, typically with the support of some aftercare services. In practice, patients at a vulnerable time are often "lost" from any support system during this transition. The hospitals surveyed for this study differed significantly both in the extent to which they viewed aftercare as their responsibility and in the efforts they devoted to follow up patients after discharge from the hospital.

Private hospitals rely heavily on office-based practitioners to provide postdischarge care (about 50% of private facilities compared with 5% of public ones). Despite this practice, 72% of private nonprofit facilities and 65% of for-profit ones said they have a particular staff member or department whose primary responsibility is ensuring that the patient's aftercare is provided. Overall, about half of the hospitals (46%) reported that they followed patients for 1 week or less, although 15% said they monitored patients' status for up to 1 year. Specialty facilities typically monitored patients longer than general hospital psychiatry units ($p \leq 0.0001$); nearly half (47%) of the nonprofit specialty hospitals monitored patient status for 6 to 12 months, compared with 14% of the nonprofit general hospitals.

Community Services

With the increased provision of care by investor-owned, multihospital systems, some observers predicted a decrease in the degree to which these hospitals would address local community needs, since they might be responsible to a corporate central office located outside the community (32). Such hospitals might discontinue unprofitable services, avoid working with preexisting public providers, or fail to provide services of community-wide benefit, like medical education or emergency services. Indeed, in 1984 we found that for-profit psychiatric hospitals were significantly less likely to offer services such as emergency care or telephone hotlines, services that had widespread community benefits but which tended to be unprofitable to operate because they are used by those the hospital is unable to bill for care (33). To address this question further, we asked questions about these unprofitable services.

Results generally confirmed the reduced involvement of for-profit hospitals in potentially unprofitable services. General hospitals are more likely to offer emergency services than are specialty hospitals, but for-profit hospitals are slightly less likely than nonprofit and public facilities to offer this service. A majority of all hospitals (67%) did not offer telephone suicide hotlines. Other services may be desirable for patients with chronic disorders but unprofitable because of constraints on reimbursement, such as Medicare's lifetime limits on inpatient coverage in specialty hospitals and limitations on reimbursement for case-management services that existed before 1989. Case-management for chronically mentally ill patients is an example of a service often not covered by insurance; it was offered by 50% of public specialty hospitals, 39% of nonprofit facilities, and 7% of for-profit facilities responding to the survey.

DISCUSSION

Some of the trends and behaviors reported here have clear policy implications. While the proliferation of private psychiatric hospitals and units in general hospitals has certainly increased geographic accessibility for some, increased screening of unprofitable patients has almost certainly reduced access to care for others. Changes in ownership and market conditions will also affect patients differently according to diagnosis. Chronically ill patients are increasingly less likely to be admitted to private facilities. The expanded role of proprietary hospitals appears to have increased access for children and adolescents, a long-underserved population (34). But because this population is also at some risk for excessive institutionalization, this expansion also raises concerns about potentially unnecessary hospitalization, particularly since these facilities conduct relatively limited review of the appropriateness of admissions (21).

In 1988, according to our data, there was a highly diversified system of funding for psychiatric inpatient services and considerable variation among types of facilities, with government sources (including Medicare and Medicaid) paying for a larger share of service both in public and private sectors than they did 5 and 15 years ago (6, 35). There have been large increases in payments to all facilities by Medicare and Medicaid since 1975, and especially in the proportion of revenues in public mental health facilities from Medicaid—a steady increase from 3% in 1975 to 8% in 1980, 18% in 1983, and 23% in our study. Similarly, the proportion of revenues from Medicare in these facilities has tripled over the same period, from 6% to 18%. These changes are remarkable in light of exclusions and restrictions of psychiatric service reimbursements under Medicaid (36).

There has been a general improvement over the past 10 years in the patient-to-professional staff ratios in all hospitals, suggesting an improvement in the quality of care. Unfortunately, we do not have data on the treatment activities of these staff. This improvement may be related to a more abundant supply of psychiatrists and psychologists, a trend that has been underway since the mid-1950s. According to data assembled from various sources by APA, between 1955 and 1983 there was a doubling of the number of psychiatrists and a quadrupling of the number of psychologists and social workers. These gains hold when adjusted for growth in the general population. These APA sources also confirm that an increasing proportion of psychiatrists, nearly 20%, report a hospital as their primary employment setting (APA Office of Research, unpublished data, 1990). The increases in psychiatrists and nurses, however, suggest an increasing medicalization of psychiatry, especially in general hospitals. The relative merits of this change remain a much debated aspect of mental health policy, but medicalization is seemingly associated with the spread of both for-profit and general hospital psychiatric care. It logically may be driven also by scientific advances in treatment for psychiatric disorders.

This medical model is seen most strikingly in the staffing profile of all (and especially proprietary) general hospitals. A prominent role was played by psychiatrists in private practice in patient care, in follow-up, and as a source of referrals. This defines a different sense of community relationship, one tied to the private psychiatrists in the community rather than to other community agencies. Whether this makes these hospitals more or less responsive to broad community needs is unclear, although the data presented here seem to favor the latter interpretation.

We think the changes observed are driven simultaneously by clinical needs of the population, government policies, and economic incentives. While previous studies have documented the singular impact of facility type and ownership, we believe an interactive model more accurately reflects the complex environment in which psychiatric care is provided. There are numerous other factors such as local competition and state policies governing uncompensated care that greatly affect the structure of the mental health care system and thus influence access to, and the process of, psychiatric care. The futurist Naisbitt (37) has described privatization of welfare services as one of the 10 major directions of societal change to expect by the beginning of the twenty-first century. Clearly, this general movement also will have an impact on mental health care.

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Disturbed Body Image in Patients With Eating Disorders

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Objective: The authors attempt to answer the question of whether patients with eating disorders experience more distortions in body image than do individuals without eating disorders. Method: The study group was composed of 214 women out of 230 patients consecutively admitted to an inpatient eating disorders program. Twelve men and four patients with atypical eating disorders were excluded from study. The 214 patients were divided into three groups: 87 with anorexia nervosa alone, 72 with anorexia and bulimia nervosa, and 55 with bulimia nervosa alone. The comparison group was composed of 61 women drawn from 125 consecutive participants in a survey of university students. Fifty-six men were dropped from the comparison group, along with eight women who fulfilled diagnostic criteria for eating disorders. Each subject used a three-dimensional measure to rate her body size and stated her desired body size at seven points: left biceps, left calf, left thigh, waist, abdomen, hips, and bust. The subjects' measurements at each of these points were taken. Distortion in body image was calculated as the subject's perceived body size divided by her actual body size. All subjects were also given a battery of tests of intelligence, skill, and memory. Results: All three patient groups differed significantly from the comparison group in distortions in body image. Most but not all patients with eating disorders had distortions in their body image. Conclusions: If replicated, these findings would suggest that the diagnostic criteria regarding disturbance of body image for both anorexia and bulimia need to be revised.

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The second criterion for the diagnosis of anorexia nervosa in *DSM-III* is "disturbance of body image, e.g., claiming to 'feel fat' even when emaciated" (p. 69). *DSM-III-R* places as the third criterion for this diagnosis an expanded description: "Disturbance in the way in which one's body weight, size, or shape is experienced, e.g., the person claims to 'feel fat' even when emaciated, believes that one area of the body is 'too fat' even when obviously underweight" (p. 67).

In the eating disorders literature, there is continuing controversy over whether disturbance in perception of body image is a necessary and always present attribute of anorexia nervosa. Crisp (1) did not deny some distortion in the anorexic patient's perception of her body size but stated that the anorexic patient does not differ greatly from the majority of adolescent girls who are not obese in a medical sense, but who report that they consider themselves fat and overestimate the degree of their overweight in terms of their shape and size. Crisp suggested that the gross overestimates which characterize many patients with anorexia probably owe this extra distortion to factors such as their wish to be thought of as physically normal and their terror that they could become truly obese if they cannot continue to curb their eating.

Garner and Garfinkel (2) stated that the distorted perceptions of body image among patients with eating disorders range from mild to severely delusional. This would seem to leave little question that the patient with an eating disorder has a distorted body image. Garner and Garfinkel suggested that assessing the degree of distortion in body image is most important because outcome research indicates that those anorexic individuals who persistently maintain the cognitive distortion that they are terribly fat, despite their emaciated condition, show the poorest improvement with treatment.

The tendency for patients with anorexia to overes-

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Detailed tables and figures for the data given here are available on request from Dr. Emerson.

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timate their body size was first reported by Bruch (3). Many studies (4–12) have substantiated this finding. Hsu (13) questioned the validity of the evidence for distortion in body image. Garner and Garfinkel, however, cited their finding that self-overestimation is highly predictive of poor prognosis at 1-year follow-up (2, p. 22) as reinforcing the presence and usefulness of the concept.

There is confusion surrounding the overlap between anorexia nervosa and bulimia. *DSM-III* treated them as separate disorders and stated specifically that "the bulimic episodes are not due to Anorexia Nervosa or any known physical disorder" (p. 69). *DSM-III-R* changed "bulimia" to "bulimia nervosa." Some clinicians, however, refer to "bulimarexia," a term that Hilde Bruch, according to Garner and Garfinkel (2, p. 12), called a semantic atrocity because it indicates that the two conditions are nearly identical, which they are not. Bruch expressed doubts that bulimia is a clinical entity. Compulsive overeating may occur, but in varying conditions and with different severity. Following this philosophy would suggest that *DSM* manuals should not list the condition at all. In an earlier book, Garfinkel and Garner (14) used elaborate clinical findings as a basis for their conclusion that patients with restricting anorexia and those who later develop bulimia are different.

DSM-III (pp. 70–71) listed five major criteria for the diagnosis of bulimia but did not mention body image. *DSM-III-R* (pp. 68–69) amplified the criteria with "persistent overconcern with body shape and weight" but did not mention distorted image of body size.

In an attempt to determine whether patients with eating disorders have distorted body images, this study focuses on similarities and differences in perceived, desired, and actual body image, measured in three and two dimensions.

METHOD

The original study group was composed of 230 consecutive admissions to an inpatient eating disorders program. Four patients with atypical eating disorders and 12 men were dropped from the study. The remaining 214 patients were divided into three groups according to *DSM-III-R* criteria: patients with anorexia nervosa only (N=87), patients with anorexia and bulimia nervosa (N=72), and patients with bulimia nervosa only (N=55).

The comparison group was drawn from 125 consecutive participants in a survey of university students in freshman English classes. The return rate of the questionnaires was 71% (125 returned out of 175 distributed). Eight women were excluded from the comparison group because their Eating Attitudes Test scores (15) were higher than 35 and they fulfilled diagnostic criteria for an eating disorder. Fifty-six men were also dropped from study, leaving a comparison group of 61 women.

Each subject's ideal body weight was identified by using the 1959 Metropolitan Life Tables (16). Tests were conducted during the first few days of hospitalization.

All patients and comparison subjects were asked to look at their bodies and then adjust a tape measure marked in centimeters so that the circumference of the tape was equal to the circumference of their bodies at seven points: left biceps, left calf, left thigh, waist, abdomen (defined as the "largest point between rib cage and hips—what most people call the stomach"), hips, and bust. Subjects estimated each point twice, one time opening the tape to the selected circumference and the other time closing the tape. The mean of the two was used as the subject's perceived body size. Subjects were then asked to select their desired body size at the same seven points by again adjusting the tape in the same way. Actual body size was then measured. Distortion was calculated as perceived body size divided by actual body size.

In addition to perceived, desired, and actual body size (which required three-dimensional measurements), all subjects indicated their perceived body size with a two-dimensional pen and paper test. They were given five scaled silhouettes designed to represent too thin, thin, average, overweight, and obese. They were asked to select the silhouette that best represented their present overall shape and then to indicate modifications, if needed, at seven points: biceps, bust, waist, abdomen, hips, thigh, and calf. They then selected the silhouette that best represented their desired body size and again indicated needed modifications. The subject's actual body size was rated by the clinician by choosing which of the five silhouettes best represented the subject's shape. This rating, however, was not used in the analysis reported here.

All patients were also given a battery of tests that included the WISC-R (17) or WAIS-R (18) and the Tactile Performance Test (19), the Trail-Making Test (19), the Halstead Finger-Tapping Test (19), and the Wechsler Memory Test (19).

Comparisons within the clinical groups in perceived, desired, and actual body size were obtained by Pearson product-moment correlation, and comparisons between groups (clinical or clinical and comparison) were obtained by one-way analysis of variance (ANOVA). The incidence of distortion in the clinical groups was determined by chi-square with correction for percentages. Differences between the various clinical and comparison groups on neuropsychological and intellectual variables were analyzed by one-way ANOVA, as were comparisons between those with and without distortions of body image. The scores on distortion and body image by body point of the three eating disorders groups and the comparison group were factor-analyzed. Finally, the intellectual variables (WISC-R or WAIS-R scores) of the subjects were compared with those of the standardization sample by means of a multiple analysis of variance (MANOVA), and the overall effect of eating disorders was tested by linear models procedures (Wilks's criterion, Pillai's

TABLE 1. Distortions in Body Image of Women With and Without Eating Disorders[a]

	Patients With Anorexia Nervosa (N=87)		Patients With Anorexia and Bulimia (N=72)		Paitents With Bulimia Nervosa (N=55)		Comparison Subjects (N=61)		
Body Point	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F[b]
Biceps	1.34	0.22	1.33	0.27	1.25	0.17	1.15	0.14	11.66
Calf	1.15	0.18	1.19	0.26	1.12	0.14	0.98	0.11	14.73
Thigh	1.22	0.23	1.24	0.24	1.56	0.14	1.05	0.12	12.72
Waist	1.25	0.20	1.33	0.21	1.26	0.16	1.08	0.11	23.04
Abdomen	1.16	0.19	1.23	0.20	1.15	0.16	0.95	0.12	29.70
Hips	1.12	0.17	1.19	0.19	1.13	0.13	0.94	0.10	30.26
Bust	1.10	0.14	1.17	0.18	1.13	0.16	0.96	0.13	21.02
Total	1.20	0.16	1.24	0.19	1.18	0.12	1.02	0.08	28.00

[a] Calculated as perceived size divided by actual size. For example, on average, the patients with anorexia nervosa perceived their biceps as 134% as large as they actually were.

[b] df=3, 171; p=0.0001 for each comparison.

trace, and Hotalling-Hawley trace). Throughout the study, $p<0.05$ was used as the level of significance.

RESULTS

Do individuals with eating disorders have greater distortions in body image than comparison subjects? All three patient groups were significantly different from the comparison group (see table 1). The individuals with eating disorders had greater distortions in body image than did the comparison subjects.

There was no significant correlation between ideal body weight and distortion in body image within any eating disorder group (for patients with anorexia nervosa, r=−0.31; for patients with anorexia and bulimia, r=−0.07; and for patients with bulimia nervosa, r=0.28). There were also no significant differences among the three groups of patients in mean distortion in body image for each of the seven body points (biceps, F=0.36, p=0.70; calf, F=2.84, p=0.06; thigh, F=0.12, p=0.89; waist, F=1.16, p=0.20; abdomen, F=0.27, p=0.76; hips, F=0.08, p=0.92; bust, F=0.95, p=0.39; total, F=0.65, p=0.53; all df=2, 196).

Do individuals with anorexia and bulimia differ in their distortions in body image and do they differ on measures of body image at particular body points? The distortion in body image measurements revealed no significant differences among the three groups of patients at any of the seven body points or in the mean distortion.

Do all individuals with eating disorders have distortions in their body image? Should *DSM-III-R* require a disturbance of body image for such patients, as it requires amenorrhea for all female patients with anorexia nervosa? Perception of body image was found to be normally distributed in the comparison group. However, body image perception was skewed in all three eating disorder groups. If distortion is defined as more than one standard deviation above the mean of comparison subjects, 73.6% (N=64) of the patients with anorexia nervosa, 80.6% (N=58) of the patients with anorexia and bulimia, and 72.7% (N=40) of the patients with bulimia had distortion. If distortion is defined as more than two standard deviations above the mean of comparison subjects, the percents of the three patient groups with distortions were 46.0% (N=40), 63.9% (N=46), and 47.3% (N=26), respectively. The percentage of patients with anorexia and bulimia who had distortions was significantly different from the percentages of the other two groups (those with anorexia only or bulimia only) (χ^2=12.79, df=2, p=<0.005).

When the two-dimensional measurement of body image was used, the three patient groups differed significantly from the comparison subjects in perceived body image when the seven body points were considered (biceps, F=2.82, df=3, 198, p=0.04; calf, F=5.61, df=3, 200, p=0.001; thigh, F=5.40, df=3, 198, p=0.02; waist, F=4.42, df=3, 198, p=0.005; abdomen, F=3.01, df=3, 200, p=0.03; hips, F=3.42, df=3, 200, p=0.02; bust, F=2.74, df=3, 198, p=0.04) but not when only the overall silhouettes were considered (F=2.19, df=3, 200, p=0.09). In addition, the desired body image of the comparison subjects was significantly larger than the desired body image of the three patient groups (F=4.73, df=3, 192, p=0.003).

Most, but not all, of the patients with eating disorders had distortions in their body image. What, if anything, was different about the patients with eating disorders who did not have such distortions?

Distortion in body image was not a function of the patient's nutritional status, as indicated by body mass index and actual weight divided by ideal body weight. Also, there was no significant correlation between amount of distortion and body mass index or actual weight divided by ideal body weight within any of the three groups (range of r=−0.04–0.12).

Differences in WISC-R or WAIS-R scores between the subjects with and without distortions in body image were noted. Comparisons of the differences between verbal and performance IQs yielded no signifi-

TABLE 2. Factor Loadings on Measures of Body Image Distortion for Women With and Without Eating Disorders

	Patients With Anorexia Nervosa (N=87)	Patients With Anorexia and Bulimia (N=72)		Patients With Bulimia Nervosa (N=55)		Comparison Subjects (N=61)	
Body Point	Factor 1	Factor 1	Factor 2	Factor 1	Factor 2	Factor 1	Factor 2
Biceps	0.5286	0.1637	0.9154[a]	0.2124	0.8564[a]	−0.0313	0.8302[a]
Calf	0.6222	0.1974	0.9073[a]	0.1983	0.8933[a]	0.0986	0.8398[a]
Thigh	0.8047	0.3640	0.8241[a]	0.4097	0.6903[a]	0.3719	0.6975[a]
Waist	0.7527	0.8014[a]	0.4739	0.7997[a]	0.3100	0.8395[a]	0.1309
Abdomen	0.8461	0.8854[a]	0.1962	0.8266[a]	0.2763	0.8173[a]	0.1502
Hips	0.7956	0.9204[a]	0.2547	0.8799[a]	0.2596	0.8484[a]	0.2682
Bust	0.7005	0.8721[a]	0.1437	0.7265[a]	0.1515	0.6372[a]	−0.0421

[a] Factor loading coefficient of variables considered per factor.

cant difference between clinical groups. However, groups with and without distortions differed significantly in verbal and performance IQs (F=14.84, df=1, 197, p=0.0002), as did the patients with anorexia only (F=10.76, df=1, 76, p=0.002) and anorexia and bulimia (F=7.29, df=1, 69, p=0.01). In all cases, the performance IQ of those with distortion was less than their verbal IQ. This suggests that in the majority of cases the patients with anorexia only and the patients with anorexia and bulimia who had distortions in body image also had lower performance IQs than verbal IQs. This would be consistent with a lowering of function related to the right cortical hemisphere. Overall, the subjects with distortions in body image had significantly higher scores on information, similarities, and vocabulary tests and lower scores on the block design test.

These findings seem to differ from those of Hamsher et al. (20), who found a relatively high rate of cognitive disturbance during the acute phase of anorexia nervosa (the point at which hospitalization was required). Those authors suggested that "anorexia nervosa in its untreated phase may itself interfere with cognition. It is presumed that the interference is brought about by metabolic disorders in the initial, emaciated state or as a result of the stress of hospitalization" (p. 86). Although we would not disagree that a state of near-starvation would be expected to decrease mental abilities, in our group of patients, who were tested upon hospitalization, those with anorexia only and those with anorexia and bulimia who had distorted body images had significantly higher scores on information, similarities, and vocabulary tests.

The results of the other neuropsychological tests were negative or equivocal except for three measures: finger tapping, dominant and nondominant hand, and tactile performance, nondominant hand. The subjects with distorted body images had more impairment on these tests. Because these tests have neuromotor components, these differences may be attributed to energy level or depression rather than a difference in function. However, the difference in the Tactile Performance Test was not seen in the dominant hand scores, suggesting right hemisphere dysfunction.

Another approach to the study of distortion in body image is to determine if the three clinical groups and the comparison group had the same factor solution or different factor solutions for the seven measures of distortion in body image. When considering the factor solution for either the clinical grouping or the distortion grouping, one is immediately struck by the commonality of the two-factor solution seen for all groups except the patient group with anorexia nervosa, which yielded a single-factor solution (see table 2). The first factor in the two-factor solution always involved the extremities: biceps, calf, and thigh. The second factor obtained contained waist, abdomen, hip, and bust—all parts of the trunk. This would suggest that the comparison subjects, the patients with bulimia only, and the patients with anorexia and bulimia, with and without distortions in body image, perceived their extremities differently from the way they perceived their trunks. Patients with anorexia nervosa only, however, had distorted images of all body points consistently, thus loading a single-factor solution.

One other approach to exploring differences in body image between individuals with and without eating disorders is to compare performance on the WISC-R or WAIS-R. On the 11 subtests of these measures, no differences were noted between or within the three clinical groups when scaled scores were analyzed by means of MANOVA. However, when the three clinical groups were compared with the standardization sample for the WAIS-R (N=1,880, representing a much larger comparison group than the comparison sample in this study), a significant difference was noted. This would suggest that the WISC-R or WAIS-R profile for women with eating disorders is different from the standardization sample of the WAIS-R. The general linear models procedure suggested that this difference was true for all of the tests except for the information (F=0.56, p=0.64), arithmetic (F=0.21, p=0.89), and object assembly (F=0.45, p=0.72) tests (all df=3, 2037). This simply means that the mean performance of the clinical groups on these three tests did not differ from that of the standardization sample. Wilks's criterion (F=3.26, df=9, 112.10, p=0.002), Pillai's trace (F=2.94, df=9, 144, p=0.003), and the Hotalling-Hawley trace (F=3.48, df=9, 134, p=0.0007)—all measures of the hypothesis of no overall eating disorder effect—yielded probabilities demonstrating that the differences noted were due to having an eating disorder. Thus, all of the analyses would suggest a profile difference between our subjects with eating disorders and the standardization sample.

DISCUSSION

This study indicates that individuals with eating disorders have greater distortions in their body image than do comparison subjects. This was true whether the patients had anorexia nervosa or bulimia nervosa alone or both conditions. Differences were seen in both three-dimensional and two-dimensional measures of distortion when specific body parts were considered. According to the overall two-dimensional measure, however, distortions among patients with eating disorders did not differ from those among the comparison group. This finding may help to explain some of the controversy in the literature.

Most but not all of the patients with eating disorders had distortions in their body image. Patients with distorted images seemed to have greater impairment on indicators of right hemisphere/parietal lobe functioning. This is consistent with the descriptions from clinical neurology of nondominant parietal lobe syndromes (21) in which patients can recognize a body part but may not believe the part is their own.

Another possible explanation for the pattern of WAIS-R and WISC-R scores is that tests of similarities and comprehension measure more abstract abilities and that tests of object assembly, arithmetic, and information are more factual and concrete. Patients with eating disorders could be considered to have problems in dealing with the factual or concrete, especially their eating and their body image.

The finding in this study that patients with bulimia nervosa had distortions in body image to the same degree as did those with anorexia nervosa needs further study. If it is replicated, it would suggest that the diagnostic criteria for both eating disorders need to be revised regarding disturbance of body image.

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A Survey of Canadian Psychiatric Residents Regarding Resident-Educator Sexual Contact

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Background and Method: A survey of all Canadian psychiatric residents was undertaken to ascertain the prevalence of resident-educator sexual contact in training programs, the residents' feelings about this contact, their knowledge of the ethical standards of the profession, and the extent of the information they had been given about this subject. An investigator-designed questionnaire was circulated to all psychiatric residents in Canada through the directors of postgraduate training programs. To ensure confidentiality, the residents returned their questionnaires directly to the investigators. Results: Of the 314 respondents, 4.1% (N=6) of the female residents and 1.2% (N=2) of the male residents reported sexual involvements with their educators. Although the majority of these eight residents had positive or neutral feelings about the contact, 37.5% (N=3) of the involved residents had mixed feelings. The residents' education concerning resident-educator sexual contact was strikingly sparse. Conclusions: This study highlights the need for inclusion of this issue in residency programs.

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Although patient-therapist sexual contact was long a neglected and controversial subject, there have been a number of studies on it in the past 10–15 years (1–4). Research in this area has led to policy statements by both APA and the Canadian Psychiatric Association explicitly prohibiting this behavior and labeling it as unethical. Of equal importance, this research has led to an increasing awareness and exploration of the psychodynamics involved in the therapeutic relationship and the potential for abuse of power that is inherent in it.

A related issue, because of the similar potential for inequity in the relationship, is sexual contact between educators and students. In a survey of the psychotherapy division of the American Psychological Association, Pope et al. (5) found that 10% of the respondents reported sexual contact with their educators when they were students and that 13% reported entering sexual relationships with their students after they became educators. There were significant gender differences in both instances. Sexual contact when they were students was reported by 16.5% of the women and 3% of the men; conversely, 19% of the men, compared to 8% of the women, reported such contact when they became educators. They also noted a "modeling effect"; women who as students had engaged in sexual contact with educators were significantly more likely to later become sexually involved with their patients. The sample of men reporting sexual contact with their female educators was too small to make any statement regarding their future behavior.

Robinson and Reid (6) surveyed a random sample of female psychologists and found that sexual contact with an educator was reported by 13.6% of the respondents. In addition, 48% of the respondents reported some kind of attempted seduction by at least one educator during their student years. Subsequently, Glaser and Thorpe (7) found that 22% of recent clinical psychology graduates had been sexually involved with their educators. Interestingly, the perception of the sexual experience with an educator became more negative with the passage of time; that is, when they were surveyed, respondents described their sexual involvement as substantially more exploitive and unethical than they had felt it to be during the experience.

In the only nationwide survey of U.S. psychiatric residents in their final year of training, Gartrell et al. (8) reported that 4.9% of the 548 respondents had been sexually involved with their educators. They found no gender difference among those who had become involved, although the age difference was noteworthy. In involvements between male educators and

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female residents, the men were, on average, 12.8 years older than the residents, whereas for female educators involved with male residents, the age difference averaged only 3.0 years. Most residents considered sexual contact to be inappropriate and harmful to an ongoing work relationship, but the majority (79.4%) considered such contact permissible if there was no current work association. Few residents (<1%) felt thoroughly educated about resident-educator sexual contact, a figure similar to that reported for psychology students (3%).

The present study was a national survey of all Canadian psychiatric residents. It was designed to gather information about both the incidence of residents' sexual contact with educators and the education they had received about such relationships in postgraduate education programs.

METHOD

We designed a questionnaire that was circulated to all psychiatric residents in Canada. A number of items were modified from a similar questionnaire designed by Gartrell et al. (8). Packages of questionnaires and a covering letter were sent to directors of postgraduate training for distribution to the residents in their programs. To ensure confidentiality, the residents returned their questionnaires directly to the investigators in self-addressed, stamped envelopes.

The questionnaire had 16 items concerning the resident's age, sex, year of training, sexual orientation, knowledge of the ethical standards of the Canadian Psychiatric Association regarding sexual misconduct, personal beliefs regarding sexual misconduct, and experience of sexual harassment or resident-educator sexual relationships. Two of the questions concerned the resident's education about patient-therapist or educator-student sexual contact. An additional 15 items were specifically addressed to those residents who had been sexually involved with educators. The terms "sexual contact" and "educator" were defined in the covering letter. Sexual contact was defined for the purposes of the study as "contact intended to arouse or satisfy sexual desire." A psychiatric educator was defined as a "clinical supervisor, course instructor, advisor or administrator" in the residency program.

RESULTS

Five hundred thirty-five questionnaires were distributed to all of the psychiatric residents in 16 different programs across Canada. Three hundred fourteen questionnaires were returned, yielding a response rate of 58.7%. There were 145 female and 169 male respondents. Their mean age was 31.5 years, with a range of 24–63 years. Eighty-two respondents were in their first year of training, 76 in the second, 68 in the third, and 88 in the fourth year. Two hundred ninety-six (94.3%) described themselves as heterosexual, 13 (4.1%) as homosexual, and five (1.6%) as bisexual. One hundred thirty-six (43.3%) were in personal psychotherapy.

Sixty-seven (21.3%) of the group had had no education concerning patient-therapist sex, 102 (32.5%) had had very little, and only 27 (8.6%) stated that they had had thorough teaching. Only six (1.9%) had had thorough teaching concerning resident-educator sexual contact; 204 (65.0%) had had no education and 72 (22.9%) had had little education on this matter. (These questions contained midrange choices between the extremes. Midrange responses account for the difference between the reported numbers and the total number of respondents.)

The residents were asked about the Canadian Psychiatric Association's position on sexual contact between psychiatrists and their patients. Fifty-five (17.5%) believed that it is permissible if treatment has been terminated. Twenty-six (8.3%) did not believe that this behavior is regulated by the Code of Ethics, whereas 72.6% (N=228) of the respondents believed correctly that the code states it to be unethical under any circumstance.

In terms of their own position on patient-therapist sex, 17.8% (N=56) of the respondents believed that it is permissible after termination of therapy, while 81.2% (N=255) believed that it is always unethical. Only one resident admitted to having had sexual contact with a patient. Four others did not answer this question.

Residents were also asked about the Canadian Psychiatric Association's position on sexual conduct between a resident and an educator. Sixty-one (19.4%) believed that it is permissible only if the supervisory relationship has been terminated. Three (1.0%) felt that it is permissible if the contact occurs outside of scheduled work or supervisory sessions. The majority, 57.6% (N=181), correctly believed that there are no regulations concerning this issue in the Canadian Psychiatric Association Code of Ethics.

Concerning their personal positions on resident-educator sexual contact, 3.5% (N=11) thought that it is permissible in certain special circumstances, and 2.5% (N=8) felt that it is appropriate outside of supervisory sessions. One hundred fifteen (36.6%) thought that it is permissible if the supervisory relationship has been terminated, and 25.5% (N=80) thought it is permissible if the educator is not a direct supervisor. Seventy respondents (22.3%) felt that it is unethical under any circumstance.

Sexual Harassment

Twenty-one (6.7%) of the residents (19 female and two male) stated that they had been propositioned by an educator. Fourteen (9.7%) of the female residents stated that they had been sexually harassed by an educator. None of the male residents reported harassment. One hundred thirty-five (43.0%) of the residents answered questions relating to their knowledge of sexual harassment or relationships between other residents and supervisors. Fifty (37.0%) of these knew of cases of sexual harassment, while 38 (28.1%) knew of other relationships.

Educator-Resident Sexual Involvement

Eight residents (six female, two male) reported a total of nine sexual relationships with their educators; one female resident had had two involvements. This represented 4.1% of the female residents and 1.2% of the male residents. All of the relationships were heterosexual. Five of these residents had also been propositioned by an educator, and one had felt harassed. These residents ranged in age from 28 to 42 years. One resident was in the first year, two each in the second and third years, and three in the fourth year. Four were in personal psychotherapy. Three of the eight had had no education on these matters; no one felt that his or her education had been thorough.

The educators involved ranged in age from 32 to 43 years (mode=40 years). They were from 2 years younger to 14 years older than the students with whom they were involved. Four of the female resident relationships involved educators 9–14 years older than the residents; one educator was 2 years younger. The two male residents were younger by 5 and 6 years than the educators with whom they became involved. In five cases, the educator was the individual's supervisor; in two of these cases, the educator was also the psychotherapy supervisor, and one was also a course instructor. In three cases, the educator's role was not specified. In five cases, the educator was in the same setting; in two cases the educator was located in another setting.

The contact was mutually initiated in five cases and initiated by the educator alone in four cases. The duration of the contact ranged from once only (two cases) to a committed relationship that had already lasted more than 3 years and resulted in marriage (one case). Four relationships lasted for only 3 months. In four cases the sexual contact began at work.

At the time of the study, in four cases residents reported no contact with the educator, in two there was ongoing sexual contact but no work relationship, in one there was professional but no social contact, and in two there was both work and sexual contact. Six of the residents had positive feelings about the contact, seeing it as appropriate and caring. One had mixed feelings (it was caring but harmful and inappropriate), and one person reported neutral feelings about the contact. Four felt that there was no effect on their current working relationship, three residents thought that the relationship was beneficial in that regard, and only one saw it as having a mixed effect. Taking into account all feelings about the contact, three residents felt pleased about it, three had mixed views, and two regarded the impact as neutral. No one reported any regrets. Five of the residents had not reported the contact to anyone; three had spoken to friends.

None of these residents felt resident-educator sex was unethical under all circumstances. Three (37.5%) felt that it was permissible under special circumstances or outside of supervision time. The majority believed that sexual contact might be permissible if the educator was not directly involved in the resident's supervision or if the supervisory relationship had been terminated. Six (75.0%) thought that psychiatrist-patient sexual contact was unethical under any circumstances, while one felt that it was permissible if therapy was terminated. None had had sexual contact with a patient in his or her care.

DISCUSSION

Overall, 2.5% of the Canadian psychiatric residents who responded reported sexual involvement with an educator. As in other studies, there was a preponderance of relationships between female students and male educators, although this difference was not statistically significant.

Most of these residents reported only positive or neutral feelings about the contact; only three respondents reported mixed feelings overall. It is possible, as Glaser and Thorpe (7) and Gartrell et al. (8) noted, that these judgments will become more negative over time. Rutter (9) hypothesized that women who have sex in the "forbidden zone" react like incest victims in that their sense of guilt and shame interferes with their ability to show anger. Denial is another way of dealing with an abusive experience and may, in part, account for the observed change in perception over time.

Pope (10) argued that such relationships are harmful in a number of ways. He questioned whether the power differential can ever allow the relationship to be truly a free choice for the trainee or whether the trainee would fear possible negative consequences of saying no. He also believes that sexual contact interferes with the supervisor's ability to make a fair evaluation of the student's progress. In addition, the resident's ability to openly discuss sexual attraction to patients may be hampered, and, as research indicates (5), this may increase the risk that the resident will later become sexually involved with a patient.

The question remains as to whether it is possible for resident-educator relationships to be healthy, mutually satisfactory contacts between consenting adults. Certainly, the workplace has always been a venue for meeting people and establishing intimate relationships. Nonetheless, as Rutter (9) pointed out, the potential for exploitation always exists in relationships that have an unequal power base. This possibility has led many universities to adopt the position that it is unethical for professors to have sexual relationships with students or teaching assistants, even when both consent to do so (9).

APA has also recently grappled with this issue. A new annotation concerning trainees and faculty members involved in ongoing work relationships was added to the *Principles of Medical Ethics With Annotations*

Especially Applicable to Psychiatry. This annotation notes the unequal relationship and the potential for abuse, stating that sexual involvement "generally takes advantage of inequalities in the working relationship" and therefore "may be" unethical (11). At the same time, resident representatives and others have argued that an abuse of power does not always occur and that APA should not violate individuals' civil rights by interfering in their choice of sexual partners.

The case against sexual harassment is much clearer, since, by definition, this represents unwanted contact. In this study 14 (4.5%) of the residents reported sexual harassment, and 50 others reported knowing about harassment of other residents. The fact that no male residents were sexually harassed points to the traditional imbalance of power in male-female relationships and allows one to speculate that similar dynamics might be operative here. The finding that 13.1% of the female respondents had been propositioned by educators is a strikingly high percentage and adds further weight to the societal assumption that it is somehow permissible for men to approach women in this way. Although residents would sometimes warn other female residents about a particular supervisor, they were much more reluctant to report this to anyone in authority ("It may reflect poorly." "In my case, I have been in contact with a supervisor who openly was trying to take advantage of female clinical clerks and female residents, but unfortunately he was in a very powerful position that intimidated his victims").

It is an interesting question whether the greater number of male supervisors involved in harassment and propositioning is merely a reflection of the larger number of men in positions of authority in teaching programs. It remains to be seen whether women will assume this exploitative aspect of power as their numbers continue to increase in the academic ranks or whether the societal prohibitions against women being sexually aggressive or becoming involved with younger or less powerful men will have a moderating effect on this development.

Residents who became involved were not different from those who did not in terms of their views regarding patient-therapist sexual relations and resident-educator sexual contact. Most residents agreed that sexual contact with a patient is unethical under any circumstances, although a substantial minority (17.8%) believed that it is permissible if therapy has been terminated. Confusion about the position of the Canadian Psychiatric Association in this regard was reflected by the varying responses, including those of the 8.3% of the respondents who believed that this behavior is not regulated by the Code of Ethics. In fact, the Canadian Psychiatric Association recently published a position paper denouncing sexual contact between psychiatrists and their patients (12). Prior to this, the *Canadian Medical Association Code of Ethics Annotated for Psychiatrists* explicitly prohibited such contact (13). The issue of posttermination involvement has not been addressed.

The majority of the respondents (57.6%) rightly believed that there are no regulations in the Canadian Psychiatric Association Code of Ethics regarding student-educator sexual contact. However, even without the benefit of regulations, most residents seemed to think that coexisting supervisory and sexual relationships may pose difficulties. Only 6.0% of the respondents felt that such relationships may be permissible. On the other hand, the majority of the respondents (62.1%) felt that sexual contact might be permissible if the work relationship had been altered from one of direct supervision or had been terminated altogether. Sexual harassment is not included in the Code of Ethics, since it is prohibited by Canadian law.

In summary, it is obviously dangerous to generalize or expound dogmatic principles in areas as complex as power and sexuality. As the motivation for sexual harassment and sexual propositioning is not necessarily the same as the motivation for sexual intimacy, it is important to differentiate between them when assessing the effect on the resident. However, it may be naive to assume that there is no common ground. In addition, there are data which suggest that a "modeling effect" is possible (5) and that residents who become sexually involved with supervisors may be more likely to engage in similar behavior with their patients at a later date.

It is the obligation of residency training programs to provide the opportunity for frank discussion of this subject, thereby allowing residents to make a more informed choice about this kind of involvement. In addition, safe, definite routes of reporting sexual harassment should continue to be established to help alleviate the burden that falls on the resident in these circumstances. Although education of residents is crucial in these matters, it is the educator who must assume ultimate responsibility. Continuing education and clear departmental policies concerning sexual contact are necessary to ensure the protection of residents during the vulnerable training period. Above all, professional integrity and ethical accountability are not only learned through the intellectual examination of issues but incorporated by example. The supervisory relationship in resident education deserves careful scrutiny in this regard.

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The Effect of Financial Management on Alcohol-Related Hospitalization

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Objective: Treatment-unresponsive alcoholics in New Zealand who are unable to care for themselves tend to be hospitalized for lengthy periods of time. The author examined the effect of adding financial management to the therapeutic management of such patients. The null hypothesis was that this would have no effect on the duration of alcohol-related hospitalization. Method: All 61 alcoholic patients registered with an alcohol outpatient clinic who received financial management over a period of 6 years were included in the study. Their alcohol-related disabilities were so severe that they had resulted or were likely to result in lengthy or frequent periods of hospitalization. The financial management involved putting each patient's income into a checking account for which a budget advisory officer was cosignatory for withdrawals. The advisor saw to it that patients' basic living requirements were being met and that expenditure on alcohol was not having a detrimental effect. Participation was voluntary for voluntary patients and involuntary for committed patients. The durations of each patient's alcohol-related hospitalizations were compared for two equal periods of time before and after financial management was instituted. Results: The null hypothesis was not supported. The duration of alcohol-related hospitalizations after financial management was instituted was 86% less than it was before such management. Conclusions: For the patient who is struggling in the face of excessive drinking to cope with the tasks of daily living, including the provision of adequate shelter and nutrition, the benefits of adding financial management to other therapeutic strategies should be considered.

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In New Zealand, when individuals with alcohol abuse or alcohol dependence fail to respond adequately to treatment and become unable to care satisfactorily for themselves, they tend to be hospitalized for lengthy periods of time rather than being allowed to live rough on skid row. However, this is expensive and may lead to institutionalization, and resources are limited. I examined the effect of adding financial management to the therapeutic management of treatment-unresponsive alcoholics, the null hypothesis being that this would have no effect on the duration of alcohol-related hospitalization.

METHOD

All 61 alcoholic patients who received financial management during the period from Dec. 1, 1983, to Sept. 1, 1989, were included in the study Eight (13%) of the patients were women and 53 (87%) were men; their mean±SD age was 57±11 years (range=30–74 years). Their alcohol-related disabilities were of such severity that they had resulted or were likely to result in lengthy or frequent periods of hospitalization with a total duration of 100 days The 61 patients represented 1.6% of the 3,725 patients registered with an alcohol outpatient clinic and came from a catchment population of 300,000. Thus, the rate for receiving financial assistance was two per 10,000 population. Forty-five of the patients had *DSM-III-R* or *ICD-9* diagnoses in addition to alcohol abuse or dependence (six patients had two additional diagnoses): 21 patients had alcohol amnestic disorders, eight had major depressive episodes, eight had personality disorders (seven antisocial and one schizoid), four had dementias associated with alcoholism, two had grand mal epilepsy, two had subdural hematomas, two had mild mental retardation, one had Wernicke's encephalopathy, one had alcoholic hallucinosis, one had undifferentiated schizophrenia, and one had bipolar disorder, manic. Forty-nine of the patients had been committed to the hospital.

The aim of the financial management was seeing

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that basic living requirements were being met and that expenditure on alcohol was not having a detrimental effect. Patients' individual budgets were calculated and arrangements made for the supply of such services as board, rent, electricity, telephone, television, restaurant meals, groceries, tobacco, clothing, bus tickets, dry cleaning, dental care, general practitioner services, newspapers, tickets for sporting and cultural events, glasses, home appliances, and haircuts. The administration varied with the resources available and the patients' requirements, but, from Jan. 1, 1988, most of the service was provided by a half-time budget advisory officer whose funding came through a disability allowance of $12 weekly paid by the Department of Social Welfare for each person receiving the service. Each patient's income was received into a checking account for which the budget advisory officer was cosignatory for withdrawals. Participation was on a voluntary or involuntary basis. Involuntary participation came with committal under the Mental Health Act of 1969 or a court order under the Protection of Personal and Property Rights Act of 1988.

A mirror-image study design used each patient as his or her own control. The duration of each patient's alcohol-related hospitalizations, obtained from hospital records, was compared for two equal periods of time, before and after financial management was instituted. A two-tailed two-group t test (1) and calculation of the point biserial correlation coefficient r_{pb} (2) were used to test the statistical significance of differences. Before the group means were compared, testing for the equality of the variances was done by using the variance ratio or F test (1), where $F=s_1^2/s_2^2$. Since this showed a significant difference between the two variance estimates, the special procedure recommended by Bailey (1) was followed in which a *d* was calculated but treated as being distributed approximately like Student's t with *df* degrees of freedom, where

$$d=x_1-x_2/\sqrt{s_1^2/n_1+s_2^2/n_2}\,;$$
$$df=1/u^2/n_1-1+(1-u)^2/n_2-1;$$
$$u=s_1^2/n_1/s_1^2.$$

Thus, the number of degrees of freedom differed from n_1+n_2-2. Cross-checking of the duration of hospitalization was done by consulting several sources, including the case record, ward register, and hospital files, but no formal reliability studies were conducted.

RESULTS

The total mean±SD duration of hospitalization before financial management was instituted for these patients was 823±1,133 days (range=9–6,287 days). The duration of financial management was 1,056±683 days (range=4–2,033 days). The duration of hospitalization during financial management was 39±64 days (range=0–323 days). The duration of hospitalization during an equal period immediately before financial management was instituted was 285±411 days (range=0–1,795 days). Thus, the duration of alcohol-related hospitalization was reduced by 86% after financial management was instituted ($t=4.61$, $df=50$, $p<0.0001$, $r_{pb}=0.55$, proportion of variance accounted for=30%). The reduction was even greater (90%) when only the 49 patients who had reached a stable rate of hospitalization (each of these patients had been hospitalized previously for 100 or more days) were considered. The duration of these patients' hospitalization during financial management was 33±57 days (range=0–323 days); during an equal period of time immediately before financial management was instituted their duration of hospitalization was 346±436 days (range=0–1,795 days) ($t=4.98$, $df=50$, $p<0.0001$, $r_{pb}=0.58$, proportion of variance accounted for=33%). The null hypothesis was not supported.

DISCUSSION

Alcohol use may be associated with conditions such as alcohol amnestic disorder, dementia associated with alcoholism, and an intermediate brain syndrome (3), which may cause cognitive impairment of such severity that the provision of financial management might be considered. Ethically, the voluntary patient's participation in such management requires informed and formal consent. For the involuntarily committed patient, participation requires a court order after due consideration has been given to the principles involved, including autonomy and beneficence. The principle of autonomy—that, provided his or her actions do not infringe on the autonomous actions of others, a person should be free to perform whatever action he or she wishes, even if it involves serious risk for the person and others consider it foolish—should not be interpreted as either absolute or too broad in scope (4). Some persons, because of incapacity, are not in a position to act in a sufficiently autonomous manner, and the actions of such nonautonomous persons may be validly obstructed in order to protect them from harm that might result from their own actions (4). The principle of beneficence requires the provision of benefits as well as a balancing of benefits and harm (4). Protecting patients against the consequences of their own choices—paternalism—poses moral questions because it involves the claim that in some cases beneficence should take precedence over autonomy (4). It has been concluded (4) that weak paternalism, in which the person whose wishes or actions are overridden has some diminished capacity (as might occur with depression or drug addiction, when the conduct involved is substantially nonvoluntary), is a coherent and defensible moral position, although it applies only to a narrow range of instances where the patients are clearly endangered.

In helping patients with psychiatric disabilities to manage in the community, Stein and Test (5) noted that the ability to budget money was important in order to obtain the required material resources such as food, shelter, clothing, and medical care. The present study is a logical extension of this work to the management of patients with alcohol-related disabilities. For the patient who is struggling in the face of excessive drinking to cope with the tasks of daily living, including the provision of adequate shelter and nutrition, the benefits of adding financial management to other therapeutic strategies should be considered.

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Drug Abuse in Schizophrenic Patients: Clinical Correlates and Reasons for Use

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Objective: This study aimed to 1) determine substance abuse prevalence and preference in a diverse sample of schizophrenic, schizoaffective, and schizophreniform inpatients, 2) compare drug-abusing and non-drug-abusing patients on demographic and clinical variables during the acute and stabilization phases of their hospital course, and 3) obtain data from patients on reasons for drug abuse and on acute state-related changes during periods of intoxication. Method: Eighty-three psychotic inpatients consecutively admitted to a New York City teaching hospital were evaluated. Sixty-eight had schizophrenia, 12 had schizoaffective disorder, and three had schizophreniform disorder diagnosed according to the Structured Clinical Interview for DSM-III-R. Each patient received ratings on the Brief Psychiatric Rating Scale, the Global Assessment Scale, and the Scale for the Assessment of Negative Symptoms at admission and at discharge, an evaluation of premorbid adjustment, and an extensive interview on drug and alcohol use. Results: Forty (48%) of the patients received diagnoses of drug or alcohol abuse or dependence. The drug-abusing patients primarily used cannabis (N=26), alcohol (N=21), and cocaine (N=14) and reported that they abused drugs to get "high," to relieve depression, and to relax. They had significantly fewer positive and negative symptoms at discharge, better sexual adjustment and worse school performance during adolescence, and more family histories of drug abuse than the non-drug-abusing patients. Conclusions: Schizophrenic patients who abuse drugs may represent a subgroup of patients with better prognoses and less severe clinical characteristics of schizophrenia, but their drug abuse may adversely affect global outcome.

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A substantial portion (15%–60%) of schizophrenic patients abuse psychoactive drugs (1–4). While clinicians have become increasingly aware of the scope of the problem, little is known about the clinical epidemiology and causes of substance abuse in schizophrenic patients. Such information may be clinically useful and perhaps offer insight into the heterogeneity and pathogenesis of schizophrenia.

Several models have been proposed to explain the frequent comorbidity of substance abuse and schizophrenia. The vulnerability model hypothesizes that drug abuse may cause schizophrenia or increase the likelihood of its expression in an already vulnerable individual. McLellan et al. (5) found that amphetamine abusers studied over 6 years were significantly more likely than barbiturate abusers to develop psychotic disorders. Andreasson et al. (6) reported that Swedish conscripts who were high consumers of cannabis had a relative risk of schizophrenia that was six times that of nonusers. It has been found that drug-abusing schizophrenic patients are younger (1, 2, 7), have the onset of schizophrenia at earlier ages, and have better premorbid adjustment (8–11) than non-drug-abusing schizophrenic patients—findings suggesting that drug abuse may trigger the development of schizophrenia.

A second model postulates that drug-abusing schizophrenic patients may be self-medicating their symptoms. This model implies a selective matching of specific substances (and their subjective effects) with specific symptoms, a match that may have informative psychobiological origins. For example, drug abuse may be understood as an "on-the-street" parallel to

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the laboratory finding that amphetamine challenge tests improve the mood and increase the work efficiency of some schizophrenic patients (12–14). A review of retrospective studies (15) has suggested that schizophrenic patients prefer drugs which might counteract negative symptoms (e.g., cocaine, cannabis, amphetamines, and hallucinogens) rather than potentially depressant drugs, such as sedative-hypnotics, opiates, and alcohol. A third, related model postulates that drug-abusing patients self-medicate uncomfortable neuroleptic-induced extrapyramidal symptoms (3, 15, 16). Anecdotal reports support the notion that schizophrenic patients self-medicate both negative symptoms and extrapyramidal symptoms by using psychoactive drugs (16).

Our study evaluated substance abuse in consecutively admitted schizophrenic, schizoaffective, and schizophreniform disorder inpatients. We used prospectively gathered data to conduct a multidimensional comparison of drug-abusing and non-drug-abusing patients on serial clinical dimensions. To our knowledge, no prospective study of inpatients of such size and scope has been previously reported.

The study aimed to 1) determine substance abuse prevalence and preference in a diverse sample of these inpatients, 2) compare drug-abusing and non-drug-abusing patients on demographic and clinical variables during the acute and stabilization phases of their hospital course, and 3) obtain data from patients on their reasons for drug abuse and on acute state-related changes during periods of intoxication.

METHOD

The study group consisted of 83 psychotic inpatients consecutively admitted to the New York Hospital-Payne Whitney Clinic from May 1988 to December 1988, who gave informed consent and fulfilled the *DSM-III-R* criteria for schizophrenia (N=68), schizoaffective disorder (N=12), or schizophreniform disorder (N=3). The subjects were between 18 and 55 years of age, were without documented neurologic or organic brain syndrome, and were carefully screened to rule out brief drug-related psychoses. Thirteen patients with prominent histories of drug abuse were excluded when a diagnosis of schizophrenia could not be made. Two general types of patients were thereby excluded: 1) those whose exacerbation of illness occurred in the context of substance abuse and for whom psychotic symptoms remitted and did not recur during periods of abstinence from drugs and 2) patients without abstinent periods or whose functioning during such periods could not be confidently ascertained.

All diagnostic and clinical symptom assessments were performed by an independent clinical research team using the Structured Clinical Interview for DSM-III-R (SCID) (17), the Global Assessment Scale (GAS) (18), the Brief Psychiatric Rating Scale (BPRS) (19), and the Scale for the Assessment of Negative Symptoms (20). Interrater reliability (intraclass correlation coefficient) on the negative symptoms scale and the BPRS was in the 0.85–0.88 range. Patients were assessed with the BPRS, the negative symptoms scale, and the GAS during the acute phase (within 5 days of admission) and during a period of relative stability (within 5 days before discharge).

Premorbid adjustment was evaluated by using the Cannon-Spoor et al. Premorbid Adjustment Scale (21). Premorbid adjustment and demographic and family history data were gathered through interviews with the patients and, in a majority (82%) of cases, interviews with their first-degree relatives. We used a family history data form that detailed psychosis, psychiatric hospitalizations, neuroleptic treatment, serious depression, and suicide attempts of the relatives. Family histories of psychiatric disorder and drug abuse were considered to be positive if reported by any available source.

The subjects received SCID interviews to generate *DSM-III-R* diagnoses of alcohol and drug abuse and dependence (22). Information from medical records and family members provided historical data. Any patient with a *DSM-III-R* diagnosis of drug or alcohol abuse or dependence was considered to be a drug-abusing patient. Non-drug-abusing patients had no such diagnosis (current or lifetime). Data on the reliability of the research diagnoses (the drug-abusing/non-drug-abusing distinction) were based on comparison with the diagnoses made by an independent outpatient clinician (P.J.W.). Reliability was good (kappa=0.80), with an estimate based on 30 cases. The clinical assessor who collected drug abuse data was blind to other clinical assessments and biological measures.

Patients who met the criteria for *DSM-III-R* drug or alcohol abuse or dependence within the 6 months before assessment were defined as recent drug abusers. Drug-abusing patients in remission were considered past drug abusers.

All patients received a semistructured drug abuse interview created for our study (23). Polysubstance-abusing patients' subjective reports of acute drug effects were generally collected for no more than two drugs. The reliability of the interview is currently being assessed for schizophrenic and borderline patients.

To assess the nonspecific characteristics of the drug-abusing group, we compared the patients with any diagnosis of drug or alcohol abuse or dependence to the patients without diagnoses of abuse or dependence. In addition, we performed three sets of post hoc analyses: 1) patients who abused only alcohol and patients who abused only cannabis were compared with patients who were not drug abusers, 2) recent drug abusers were compared with past drug abusers and patients who were not drug abusers, and 3) analyses were performed excluding the atypical schizophrenic patients (schizoaffective and schizophreniform).

We analyzed the categorical data using contingency table and chi-square analyses. Continuous data were analyzed with t tests (two-tailed) and analysis of variance. BPRS composite scores of global symptom factors (anergia, activation, thought disorder, paranoia-suspiciousness, anxiety-depression) reported by Guy (24) were calculated. Data from the Scale for the Assessment of Negative Symptoms were analyzed using global summary items for each of the five scales. Our approach to dealing with the potential type I error associated with multiple tests was to perform a test of the overall significance using a composite measure, as recommended by Cohen and Cohen (25). Only in the case of a significant result ($p<0.05$) for the composite did we perform tests of significance for subscales. Subjective effects data were analyzed by using a 3 (group) ×3 (response category) chi-square. We performed post hoc analyses among the groups if an overall significant ($p<0.05$) chi-square was obtained.

RESULTS

Demographic and Substance Abuse Variables

There were no statistically significant differences between the drug-abusing and the non-drug-abusing patients on the demographic variables of age, sex, race, marital status, living arrangements, education, and occupational functioning. The patients were young (mean±SD age=30.6±8.5 years), were unmarried (70%, N=58), and had at least a high school education (78%, N=65). Sixty-three percent (N=52) were white. Age at onset of schizophrenia (mean±SD=22.9±7.4 years) and number of previous hospitalizations (mean±SD=2.7±3.3) did not differ between the two groups. The mean±SD age at onset of alcohol use was 19.5±4.7 years; age at onset of drug use was 18.9±4.8 years.

Forty (48%) of the 83 patients received *DSM-III-R* diagnoses of drug abuse or dependence and met the criteria for a total of 76 diagnoses (cannabis, 26; alcohol, 21; cocaine, 14; hallucinogens, five; stimulants, five; sedative-hypnotics, three; other, two). The majority of the diagnoses were for dependence (N=64) rather than abuse (N=12). Nineteen patients (23%) used one substance only (cannabis, eight; alcohol, 10; stimulants, one), while 21 patients (25%) were polysubstance users. Twenty-nine (35%) of the patients were recent users. Table 1 shows the number of days within 1 week, 1 month, and 1 year before admission that recent drug abusers used alcohol, cocaine, and cannabis. Twenty-nine (48%) of the drug-abusing patients' 61 diagnoses of cannabis, alcohol, or cocaine abuse or dependence reflected daily drug use for 2 or more years. Another 12 diagnoses (20%) reflected use three times a week for 2 or more years.

Twenty-six (65%) of the 40 drug-abusing patients had family histories of substance abuse in first-degree relatives, compared with five (12%) of the 43 non-drug-abusing patients ($\chi^2=9.88$, df=1, $p<0.01$). In contrast, there were no significant differences in family history of psychiatric illness, hospitalizations, or suicide attempts between the drug-abusing and non-drug-abusing schizophrenic patients.

TABLE 1. Alcohol, Cannabis, and Cocaine Use by Recent Drug-Abusing Schizophrenic Patients During the Week, Month, and Year Before Hospitalization

	Days of Use					
	Alcohol Abusers (N=17)		Cannabis Abusers (N=13)		Cocaine Abusers (N=7)	
Period Before Hospitalization	Mean	SD	Mean	SD	Mean	SD
Week	3.6	3.4	1.9	2.5	2.3	2.4
Month	14	11	11	11	9	10
Year	145	120	133	104	120	106

Clinical and Treatment Variables

There were no significant differences between the two groups of patients on any of the GAS, BPRS, or negative symptom measures at admission. However, at discharge the drug-abusing patients showed less severe psychopathology, as measured by total BPRS and negative symptom scores (table 2). Analysis of the BPRS factors revealed that drug-abusing patients had significantly lower scores on positive symptom BPRS dimensions (thought disorder and paranoia-suspiciousness) as well as anergia, but did not differ from the non-drug-abusing patients on activation and anxiety-depression.

When recent drug abusers, past drug abusers, and non-drug-abusing patients were compared, no differences were found at admission. At discharge the recent drug abusers had significantly lower mean±SD total BPRS scores (recent abusers, 1.87±0.52; past abusers, 1.77±0.15; nonabusers, 2.24±0.66; F=4.75, df=2, 77, $p<0.05$) and significantly lower thought disorder scores (recent abusers, 1.78±0.78; past abusers, 2.05±1.18; nonabusers, 2.46±1.16; F=4.99, df=2, 77, $p<0.01$) than the non-drug-abusing patients. Both the recent and past abuser groups had significantly lower paranoia-suspiciousness scores than the nonabuser group (recent abusers, 1.64±0.83; past abusers, 1.26±0.74; nonabusers, 2.44±1.07; F=9.81, df=2, 77, $p<0.001$).

Analysis of scores on the Scale for the Assessment of Negative Symptoms revealed that the drug-abusing patients had significantly less affective flattening than the non-drug-abusing patients (table 2). Exclusion of the atypical schizophrenic patients resulted in the finding that besides having less affective flattening, the drug-abusing patients had less anhedonia and less avolition-apathy than the patients who were not drug abusers.

The drug-abusing and non-drug-abusing patients did not differ in global functioning as measured by the GAS, mean±SD length of hospital stay (abusers, 47.4±25.7 days; nonabusers, 61.1±54.4; t=−1.45, df=81, p=0.15), and mean±SD dose of neuroleptic medica-

TABLE 2. Scores on Clinical Measures at Discharge of Drug-Abusing and Non-Drug-Abusing Schizophrenic Patients

	Drug Abusers (N=40)		Non-Drug-Abusers (N=43)		Significance		
Measure	Mean	SD	Mean	SD	t	df	p
Scale for the Assessment of Negative Symptoms[a]							
Total	2.35	0.72	2.70	0.74	2.15	79	0.03
Alogia	2.05	0.87	2.28	1.08	1.03	79	n.s.
Anhedonia-asociality	2.74	1.06	3.12	1.18	1.52	79	n.s.
Attention	1.87	1.02	2.19	1.08	1.36	79	n.s.
Affective flattening	2.40	0.91	2.80	1.01	1.96	79	0.05
Avolition-apathy	2.71	1.20	3.12	0.91	1.76	79	0.08
BPRS[b]							
Total	1.87	0.46	2.26	0.66	2.98	78	0.004
Thought disorder	1.85	0.91	2.46	1.16	2.64	79	0.01
Paranoia-suspiciousness	1.60	0.80	2.44	1.07	3.98	79	0.001
Anxiety-depression	2.42	0.71	2.29	1.00	−0.67	79	n.s.
Anergia	1.86	0.62	2.30	0.83	2.54	78	0.02
Activation	1.65	0.61	1.73	0.82	0.49	76	n.s.
GAS[c]	43.06	8.90	40.48	12.01	−1.02	72	n.s.

[a] Scores range from 0 to 5; lower scores represent less severe symptoms. The total score represents the mean of the means for the five individual items.

[b] Scores range from 1 to 7; lower scores represent less severe symptoms. Each individual score is the mean of the means for BPRS items included in that factor; the total score represents the mean of the means for the five factors.

[c] Scores range from 0 (extremely dysfunctional) to 100 (extremely high level of functioning).

tion at discharge (abusers, 554.6±389.7 chlorpromazine equivalents; nonabusers, 973.3±1607.1; t=−1.52, df=73, p=0.13). (Neuroleptic doses for eight patients were unavailable because they were participants in another blind research protocol.)

Premorbid adjustment scores revealed no differences between groups in psychosocial adjustment in childhood or adulthood. However, drug-abusing patients reported significantly better sexual adjustment and worse scholastic adaptation in early adolescence (sexual adjustment: mean±SD score for drug abusers, 1.38±1.06; for nonabusers, 2.17±1.39; t=2.16, df=58, p<0.05; scholastic adaptation: drug abusers, 2.61±1.42; nonabusers, 1.85±1.31; t=−2.16, df=58, p<0.05) and in late adolescence (sexual adjustment: drug abusers, 2.12±1.17; nonabusers, 2.53±1.60; t=2.08, df=57, p<0.05; scholastic adaptation: drug abusers, 2.74±1.32; nonabusers, 1.97±1.49; t=−1.99, df=54, p<0.05). (Lower scores indicate better functioning.) These differences were not apparent when only the schizophrenic patients were assessed.

Subjective Effects and Reasons for Drug Use

Cannabis, alcohol, and cocaine were the only drugs used with sufficient frequency to permit statistical analysis. Patients reported that all three drugs acutely increased happiness and decreased depression, but that alcohol, cocaine, and cannabis had different effects on anxiety, psychotic symptoms, and energy level (table 3). Alcohol and cannabis shared common effects of decreasing anxiety, in contrast to cocaine, which increased anxiety. Cannabis and cocaine were more often reported to increase energy and psychotic symptoms than alcohol. Table 4 indicates patients' reported reasons for use, which did not differ greatly across drugs.

DISCUSSION

This study found a clinically significant lifetime prevalence of substance abuse in a sample of consecutively admitted schizophrenic inpatients: 35% of the patients had recently used drugs to an extent that caused impairment in functioning; almost 50% of the patients had experienced some impairment due to drug or alcohol use during their lifetimes. Our data are consistent with rates of drug abuse for schizophrenic patients reported by other groups in diverse geographic locations (1–3, 9). Comparison with a 16.4% lifetime prevalence rate of *DSM-III* substance abuse disorders in a community sample from the NIMH Epidemiologic Catchment Area Program (26) suggests that the rate of drug abuse among schizophrenic patients is considerably higher than that in the general population. However, interpretation of these data is inconclusive without reference to appropriately matched control groups; the prevalence of schizophrenia, as well as substance abuse, is known to be greater among younger people. Further, data from urine drug screens, if they had been available, would have strengthened the validity of our data on current use.

Our group of schizophrenic patients commonly used cannabis, alcohol, cocaine, hallucinogens, and stimulants, corroborating the findings of retrospective studies (9, 15). In comparison with a group of 19 consecutively admitted psychotic affective disorder patients of similar age in a parallel study of similar design (G. Haas, personal communication, 1990), we found that

TABLE 3. Effects of Alcohol, Cannabis, and Cocaine Use on Mood and Symptoms Reported by Drug-Abusing Schizophrenic Patients[a]

	Effects of Drug										
	Alcohol Abusers (N=14)			Cannabis Abusers (N=23)			Cocaine Abusers (N=9)			Significance	
Dimension	Increased	Same	Decreased	Increased	Same	Decreased	Increased	Same	Decreased	χ^2 (df=4)	p
Anxiety	0	0	14	1	0	22	6	1	2	28.64	0.001[b]
Depression	1	3	10	1	3	19	2	3	4	5.14	n.s.
Calm	10	2	2	18	3	2	3	1	4	7.30	n.s.
Suspicion	1	11	2	17	5	1	3	3	2	17.66	0.001[c]
Trust	3	9	1	1	11	11	1	2	5	9.46	0.05[d]
Hallucinations	0	13	0	7	15	1	2	3	2	12.47	0.01[e]
Slowing down	7	3	3	5	2	15	0	2	6	10.65	0.03[f]
Stiffness	0	12	0	0	21	1	0	8	0	—[g]	—
Energy	3	0	11	16	1	5	8	0	1	15.54	0.004[h]

[a] Forty-six reports on the 61 instances of dependency on or abuse of these drugs were obtained. Eight reports were missing because of lack of patient cooperation, three were missing because of temporally remote drug use, and four were missing because the patients had already reported on two other drugs.

[b] Cocaine versus cannabis: $\chi^2=18.7$, df=1, $p<0.0001$; cocaine versus alcohol: $\chi^2=15.7$, df=1, $p<0.001$.

[c] Alcohol versus cannabis: $\chi^2=15.5$, df=1, $p<0.001$.

[d] Alcohol versus cannabis: $\chi^2=7.3$, df=1, $p<0.05$.

[e] Alcohol versus cannabis: $\chi^2=5.8$, df=1, $p<0.05$.

[f] Alcohol versus cannabis: $\chi^2=6.7$, df=1, $p<0.05$; alcohol versus cocaine: $\chi^2=3.5$, df=1, $p=0.06$.

[g] Chi-square not calculable because of pattern of zeroes.

[h] Alcohol versus cannabis: $\chi^2=10.9$, df=1, $p<0.01$; alcohol versus cocaine: $\chi^2=13.8$, df=1, $p<0.001$.

TABLE 4. Reasons for Drug Abuse Reported by Schizophrenic Patients With Drug-Abuse Diagnoses

	Yes		No	
Reason	N	%[a]	N	%[a]
To get high	38	72	14	26
To decrease depression	38	72	15	28
To relax	34	64	19	36
To increase pleasure	33	62	18	34
To increase energy	30	56	22	42
To go along with the group	29	55	24	45
To increase emotions	26	49	26	49
To talk more	24	45	29	55
To be more creative	21	40	31	58
To satisfy curiosity	11	21	40	75
To increase concentration	10	19	42	81
To work and study better	9	17	44	83
To decrease side effects of medication	8	15	44	83
To decrease hallucinations	6	11	46	87
To decrease suspiciousness	3	4	49	92

[a] Reports on 53 of the 61 instances of dependency on or abuse of these drugs were obtained. One report was missing because of lack of patient cooperation, three were missing because of temporally remote drug use, and four were missing because the patients had already reported on two other drugs. Where percentages do not add to 100, the remaining responses were "not sure."

our schizophrenic patients showed a relatively greater preference for psychotomimetic drugs (cocaine, cannabis, stimulants, and hallucinogens) in contrast to the more common use of alcohol and sedative-hypnotics among the affective disorder patients ($\chi^2=5.2$, df=1, $p<0.05$). Our findings add to the accumulating body of data indicating that schizophrenic patients preferentially abuse drugs that induce psychotic symptoms.

Our results suggest important clinical differences between drug-abusing and non-drug-abusing schizophrenic groups. The drug-abusing schizophrenic patients showed less overall psychopathology than the schizophrenic patients without drug abuse on measures of positive and negative symptoms at discharge, although lengths of hospital stay and amounts of neuroleptic medication were equivalent. Given that the drug-abusing patients were no different from the nonabusers in psychopathology at admission, it is possible that drug-abusing schizophrenic patients respond more quickly or completely to hospital treatment than schizophrenic patients without drug abuse. The less severe symptoms demonstrated by the drug-abusing patients may also have resulted from drug abstinence in the hospital; a variety of abused drugs have been shown to exacerbate psychosis in schizophrenic patients (1, 12–14, 27, 28), and in this study recent drug-abusing patients demonstrated significantly lower levels of positive symptoms at discharge than did patients who were not drug abusers.

Even if drug abstinence did account for the lower symptom severity among the recent drug-abusing patients, the fact that equivalent treatment resulted in lower symptom severity for past drug-abusing patients requires explanation. Perhaps the social skills and motivation necessary to obtain drugs select out the more treatment-responsive schizophrenic patients with better prognosis, who, when treated appropriately and abstaining from drugs, would be less symptomatic than non-drug-abusing patients. It makes clinical sense that patients with fewer negative symptoms would be more likely to use drugs; negative symptoms might reduce the energy and motivation required to seek and obtain drugs.

When just the schizophrenic patients (excluding atypical cases) were considered, more of the negative symptoms of the drug-abusing patients were less severe at discharge. The exclusion of schizoaffective patients' data from the analysis of negative symptoms may have reduced the possible confounding effect of depressive symptoms. Future investigations need to compare the impact of the broad and narrow definitions of schizophrenia on substance abuse patterns.

In spite of the lower severity of symptoms found in the drug-abusing patients at discharge, it is important to note that global functioning as reflected on the GAS was equivalent for the two groups. We suspect that drug abuse may impair global functioning sufficiently to compromise drug-abusing patients' possible advantage over non-drug-abusing patients in terms of less severe psychopathology.

The drug-abusing schizophrenic patients demonstrated better premorbid functioning than the patients without drug abuse on measures of sexual adjustment during early and late adolescence—a finding which confirms and extends reports of previous studies that examined adolescence (8) and premorbid *DSM-II* personality diagnoses (11). The lower scores on scholastic measures may indicate the truancy and antisocial behavior often associated with drug abuse. The superior premorbid functioning of the drug-abusing patients on social-sexual measures may indicate that schizophrenic patients with better prognostic features are more likely to have the interest and capability to seek and use drugs. It appears that the analyses of the schizophrenic patients alone did not reveal the differences found in the larger sample because of the restriction of range brought about by dropping the data of the schizoaffective disorder patients who had superior levels of premorbid functioning.

The finding that family histories of drug abuse were significantly more common in the drug-abusing than in the non-drug-abusing patients suggests that there may be familial determinants of drug abuse, which could be environmental, genetic, or both. In a study of schizophrenia and alcoholism in twins, Kendler (29) found that monozygotic twins of alcoholic schizophrenic parents were more likely than dizygotic twins of alcoholic schizophrenic parents to have both alcoholism and schizophrenia, suggesting a genetic component in both alcoholism and schizophrenia. Although our results should be interpreted cautiously because all family members were not interviewed directly and a systematic method such as the Family History Research Diagnostic Criteria procedure (30) was not used, the familial association with drug abuse in schizophrenia suggests areas for future research.

Drug-abusing patients' explanations for drug abuse suggest that schizophrenic patients may use drugs to medicate specific symptoms. Most patients reported that they used drugs to relieve depression and to relax. Responses consistent with the desire for relief of negative symptoms or depression (e.g., to increase emotions, talk more, increase energy) seemed important for about half of the patients. Relatively few patients reported abusing drugs to reduce extrapyramidal symptoms.

Drug-abusing patients' three most abused drugs (cannabis, alcohol, and cocaine) revealed distinctive patterns of effects. The most preferred drug, cannabis, was both anxiolytic and activating (increasing energy). The next most popular drugs each shared one of those favored effects: alcohol, the anxiolytic effect, and cocaine, the activating effect. Since the drug-abusing patients reported that they abused drugs primarily to alleviate depression, perhaps they construed anxiety and decreased energy (either primary or neuroleptic-induced) as depression. The disparity between patients' reports of specific drug effects and their reasons for drug abuse may give clues about how schizophrenic patients experience depression, which is known to be difficult to distinguish from akinesia (31) and negative symptoms (32) in schizophrenia.

These self-report data are limited by several important factors. The patients' explanations of drug abuse may have been post hoc rationalizations for symptoms actually caused by drug abuse. The reliability of patients' self-report data depends on reports of their feelings and experiences while intoxicated; retrospective self-report data are subject to general biases of recall and state-dependent effects. Schizophrenic patients may not differ from other populations in this regard. Nevertheless, these perceptions, however inaccurate, may themselves drive drug-taking behavior, and thus they merit further investigation. Drug-abusing patients' reports of their reasons for drug use and the subjective effects of drugs indicate that the self-medication of dysphoria might propel some schizophrenic patients to abuse drugs.

It has been reported that drug-abusing schizophrenic patients require more hospitalization (33–35), have lower compliance with treatment regimens (3, 36, 37), and are at greater risk for suicide (38). Our data show that despite decreased scores on measures of positive and negative symptoms at discharge, drug-abusing patients function no better than patients without drug abuse during the stabilization phase, suggesting that the combination of drug abuse and schizophrenia may complicate an otherwise less severe case of schizophrenia.

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Clozapine and Norclozapine Plasma Concentrations and Clinical Response of Treatment-Refractory Schizophrenic Patients

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Objective: *Clozapine, an atypical antipsychotic, has been estimated to be effective in 30% of treatment-refractory schizophrenic patients. The authors hypothesized that if a dose-response relationship was obvious for this drug, the response rate could be significantly amplified.* *Method:* *Following an 8–24-day dose titration phase, 29 inpatients with treatment-resistant schizophrenia diagnosed according to* DSM-III-R *were given a clozapine dose of approximately 400 mg/day for 4 weeks; blood samples were obtained weekly during this period.* *Results:* *A receiver operator curve demonstrated that the threshold clozapine plasma concentration for therapeutic response was 350 ng/ml. Sixty-four percent of the patients with clozapine plasma concentrations greater than 350 ng/ml responded, whereas only 22% of the patients with concentrations less than 350 ng/ml responded.* *Conclusions:* *Use of clozapine blood levels as a predictor for treatment response in treatment-refractory schizophrenic patients appears worthwhile, since the measurement's sensitivity for response was 64% and the specificity for nonresponse was 78%.*

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Clozapine, classified as an atypical antipsychotic, appears to be a major improvement in the treatment of schizophrenic patients. A large multicenter study showed that 30% of schizophrenic patients who were resistant to adequate trials of at least three antipsychotics, as well as a 6-week trial of haloperidol, improved when treated with clozapine (1). However, there have been only limited data on plasma concentrations, which might help predict which treatment-resistant schizophrenic patients may respond to clozapine. To our knowledge, only three studies have examined the relation between clozapine plasma concentrations and clinical change (2–4). Thorup and Fog (2) studied 11 chronic schizophrenic patients who had been treated for long periods with clozapine and found no correlation between clozapine plasma concentrations and clinical response. The study was not a true fixed-dose, prospective trial of clozapine. Ackenheil et al. (3) and Brau et al. (4), reporting on this relationship, suggested that the degree of improvement seen in their two studies was independent of plasma concentrations. It is not clear whether these were fixed-dose studies, although it appears that the greatest improvement in paranoia and hallucinations occurred with plasma concentrations of less than 200 ng/ml. With these limited data available, it was the purpose of this investigation to determine whether a correlation exists between clozapine concentrations and therapeutic response by administering a fixed dose of clozapine for 4 consecutive weeks.

METHOD

The patients in the study met the following criteria: 1) age greater than 18 years; 2) *DSM-III-R* diagnosis of schizophrenia; 3) three 6-week periods in the preceding 5 years of treatment with antipsychotics representing at least two chemically dissimilar classes, at a dose equivalent to at least 750 mg/day of chlorpromazine, without substantial relief of symptoms; 4) symptoms significantly severe to generate a score exceeding 40 on an 18-item anchored version of the Brief Psychiatric Rating Scale (BPRS) (5); and 5) no depot antipsychotics during the preceding 6 weeks.

Most of these patients participated in the University of Iowa Mental Health Clinical Research Center protocols, which required a 3-week drug washout. Cloza-

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pine was then initiated at a dose of 50 mg/day and increased by 50 mg/day, as tolerated by the patient, to a maximum dose of 400 mg/day. The patients were then maintained on a fixed dose of clozapine for a 4-week period. Subjects who developed adverse effects that prohibited increasing the dose to 400 mg/day were maintained on the maximum dose tolerated.

A trained research assistant reviewed all available records, administered the Comprehensive Assessment of Symptoms and History (6) within 1 week of admission, and determined a diagnosis. Without knowledge of the results of this assessment, a senior clinician and an investigator (D.D.M.) also independently reviewed medical records, conducted a brief unstructured interview, and assigned diagnoses. For a patient to be admitted to the study group, he or she had to receive independent diagnoses of schizophrenia from the assistant who administered the interview, the senior clinician, and the investigator. On the day of admission, the day before treatment began, and weekly thereafter, raters who were blind to the patients' clozapine plasma concentrations quantified symptoms using the BPRS.

Blood samples were collected in 10-ml heparinized Vacutainer tubes by antecubital puncture. Plasma was separated by centrifugation at 1500 rpm for 10 minutes and stored at 5 °C. For each sample a 4-ml aliquot of plasma was analyzed according to a modified version of the high-performance liquid chromatography method of Lovdahl et al. (7). The instrument used for assays was an isocratic Shimadzu LC-6A liquid chromatograph equipped with an ultraviolet variable-wavelength spectrophotometric detector (SPD-6A), a manual injector, and a data processor (C-R3A). A standard curve for the clozapine and its demethylated metabolite norclozapine was linear for values ranging from 50 to 1600 ng/ml. The assay was precise; coefficients of variation for six clozapine samples of 50, 150, and 300 ng/ml were 4.2%, 3.9%, and 0.9%, respectively. The corresponding figures for norclozapine at 50, 150, and 300 ng/ml were 8.6%, 14.0%, and 12.0%, respectively. The interday coefficient of variation for clozapine, 150 ng/ml, was 9.9% over the life of the assay. The recovery averaged 84.4% for clozapine and 28.4% for norclozapine. The minimum quantifiable concentration, defined as three times the standard deviation of the lowest point on the calibration curve, was 15 ng/ml for clozapine and 30 ng/ml for norclozapine.

Demographic and clinical characteristics of the responders and nonresponders were compared by using unpaired t tests. Total BPRS scores and individual BPRS factor scores were compared by using paired and unpaired t tests. Unless otherwise stated, all tests were two-tailed and an alpha level of 0.05 was considered significant. The optimum plasma clozapine and total clozapine (clozapine plus norclozapine) concentrations for response were determined by generating receiver operating curves and then testing the sensitivity finding by chi-square analysis.

RESULTS

Thirty-four patients met the inclusion criteria, provided informed consent, and were started on the clozapine regimen. Of these, 29 (85.3%) completed 4 weeks of treatment with a fixed dose of clozapine. Of the five patients who dropped out of the study, four dropped out after experiencing intolerable side effects, and one dropped out after experiencing a grand mal seizure that required the addition of phenytoin to his regimen. Of the four who dropped out of the study because of adverse effects, two dropped out after 3–5 days because of sedation and orthostatic dizziness, one dropped out after 3 weeks because of the same symptoms, and the fourth patient was discontinued, after taking clozapine for approximately 3 weeks, when he developed a fever, severe hypotension, and an elevated creatine phosphokinase level.

Of the 29 completers, 20 were male and nine were female. The mean±SD age of the group was 33.2±7.8 years, with a range of 19–48 years. The subjects received a mean±SD daily clozapine dose of 384±42 mg, equivalent to 4.9±1.0 mg/kg per day. Among the patients who improved while taking clozapine, there was no significant difference (unpaired t=1.49, df=27, p=0.15) in dose between the responders (mean±SD= 4.6±1.0 mg/kg per day) and the nonresponders (5.2± 1.1 mg/kg per day). Of the 29 patients who completed the study, 24 (82.6%) reached the dose plateau of 400 mg/day; one of the patients received 450 mg/day. The other five patients were unable to tolerate a dose of 400 mg/day. One was maintained on a dose of 350 mg/day, three on 300 mg/day, and the fifth on 250 mg/day. It required a mean±SD of 10.5±3.3 days (range=7–24 days) for the titration of the dosage to reach these patients' maximum tolerable doses. The limiting adverse effect in all five patients was daytime sedation. These doses resulted in mean±SD clozapine plasma concentrations at the end of treatment weeks 1, 2, 3, and 4 of 417±286, 349±198, 382±283, and 348±307 ng/ml, respectively. Corresponding norclozapine plasma concentrations were 130±79, 106±61, 117±76, and 111±92 ng/ml. One-factor repeated measures analyses of variance found no significant difference in the 4 weeks of clozapine levels (F=1.148, df=3, p=0.34) or the 4 weeks of norclozapine concentrations (F=1.143, df=3, p=0.34) within subjects, although differences were obvious and consistent between subjects (F=8.854, df=27, p=0.0001, and F= 6.893, df=27, p=0.0001, respectively). Intraclass correlations for the between-subjects effects were 0.89 and 0.86 for summed clozapine and norclozapine concentrations, respectively, indicating a high degree of consistency. Thus, for all subsequent analyses, the clozapine and desmethylclozapine concentrations used for each patient were the means of the levels at weeks 1, 2, 3, and 4. The mean±SD clozapine and norclozapine values were 374±233 and 116±65 ng/ml, respectively. The data describing the individual patients are presented in table 1.

TABLE 1. Data on 29 Schizophrenic Patients Treated With Clozapine for 4 Weeks

Patient	Age (years)	Sex	Length of Illness (years)	Plasma Level (ng/ml)		BPRS Score	
				Clozapine (ng/ml)	Norclozapine (ng/ml)	Baseline	Week 4
Responders (N=11)							
1	30	M	9	100	25	47	29
2	37	M	16	122	27	66	28
3	48	F	25	213	50	47	30
4	32	M	15	260	99	43	33
5	31	M	7	397	112	42	31
6	30	M	9	504	105	47	25
7	32	F	12	520	147	65	34
8	35	F	18	527	190	42	30
9	26	M	11	544	227	40	27
10	48	M	21	573	206	42	31
11	27	M	7	687	163	47	30
Mean	34.2	—	13.6	404	123	48.0[a]	29.8[b]
SD	7.5	—	5.9	199	70	8.9	2.6
Nonresponders (N=18)							
12	39	F	18	84	37	64	49
13	31	M	12	128	34	53	42
14	22	M	8	200	84	48	43
15	41	M	20	201	90	50	39
16	26	M	8	206	59	67	55
17	42	F	14	213	147	71	66
18	27	M	13	229	66	65	42
19	48	M	26	273	89	58	46
20	19	M	2	280	87	43	37
21	31	M	11	283	125	58	41
22	35	M	15	289	96	61	48
23	29	M	10	304	95	71	40
24	30	F	12	307	104	56	48
25	44	F	24	322	95	60	44
26	32	F	10	549	144	46	40
27	39	M	21	662	142	47	36
28	26	F	10	782	244	64	38
29	25	M	5	1088	272	51	55
Mean	32.6	—	13.3	356	112	57.4[a]	44.9[b]
SD	8.1	—	6.4	255	63	8.6	7.7

[a] Significant difference between responders and nonresponders (unpaired t=3.43, df=27, p=0.002).
[b] Significant difference between responders and nonresponders (unpaired t=6.31, df=27, p<0.0001).

Patients were classified as responders or nonresponders according to the criteria of Kane et al. (1). Improvement or response was defined as a 20% or greater change in the total BPRS score from baseline to the end of week 4 of fixed dosing and a final BPRS score of 34 or less. Eleven (37.9%) of the 29 patients were classified as responders by these criteria. As presented in table 1, there were no statistically significant differences in age, sex distribution, duration of illness, clozapine concentration, or norclozapine concentration between the group of responders and the group of nonresponders. However, the nonresponders had significantly higher BPRS scores than the responders both at baseline and at the end of the 4-week fixed-dose period.

Each patient's BPRS scores were broken down into three symptom factors, based on Guy et al.'s five-factor varimax solution (8), from the 18-item BPRS. The anergia factor, the thought disturbance factor, and the interpersonal disturbance factor were used in the analyses. The anergia factor was used as an estimate of the negative symptom response to clozapine, while the thought and interpersonal disturbance factors were used as indices of the positive symptom response to clozapine. Table 2 presents the factor scores for the responders and nonresponders at baseline and after 4 weeks of a fixed dose of clozapine. At baseline the nonresponders' anergia scores were greater than those of the responders, although there was no significant difference in the other two factor scores. Both the responders and the nonresponders showed significant decreases (all p values <0.05) in all three factor scores over their periods of clozapine treatment. However, at week 4 the responders' scores were significantly lower for anergia, thought disturbance, and interpersonal disturbance.

The optimal split for the clozapine concentrations was estimated by drawing receiver operating characteristic curves (9). To construct the curve, the percentage of responders in the presence of a signal ("hits" or

TABLE 2. BPRS Factor Scores of 29 Schizophrenic Patients Treated With Clozapine for 4 Weeks

	Baseline Score				Week 4 Score			
	Responders		Nonresponders		Responders		Nonresponders	
Factor	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Anergia	9.5[a]	3.0	14.4[a]	4.4	7.5[b]	2.3	10.8[b]	4.5
Thought disturbance	12.4	4.0	14.9	3.8	7.0[c]	1.8	11.6[c]	3.4
Interpersonal disturbance	7.5	3.6	10.0	3.1	4.6[d]	1.3	7.8[d]	1.8

[a] Significant difference between responders and nonresponders (unpaired t=3.18, df=27, p=0.004).
[b] Significant difference between responders and nonresponders (unpaired t=2.27, df=27, p=0.03).
[c] Significant difference between responders and nonresponders (unpaired t=4.07, df=27, p=0.0004).
[d] Significant difference between responders and nonresponders (unpaired t=5.08, df=27, p=0.0001).

FIGURE 1. Receiver Operating Curve for the Relation Between BPRS Scores and Clozapine Plasma Concentrations of 29 Schizophrenic Patients Treated for 4 Weeks

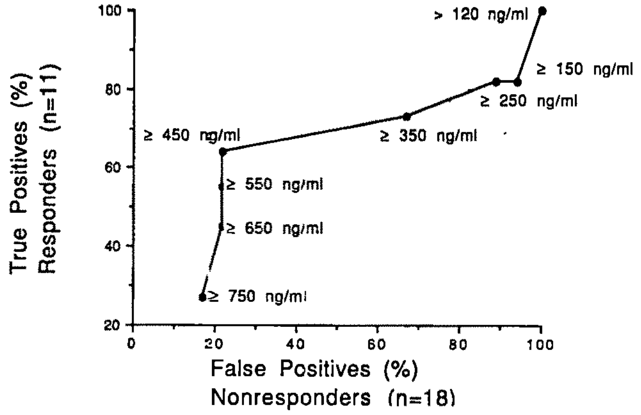
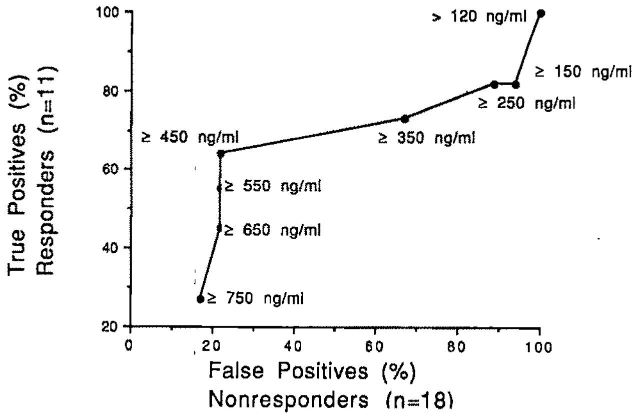


FIGURE 2. Receiver Operating Curve for the Relation Between BPRS Scores and Total Clozapine (Clozapine Plus Norclozapine) Plasma Concentrations of 29 Schizophrenic Patients Treated for 4 Weeks



true positives, i.e., responders at a particular clozapine plasma concentration range) was plotted against the percentage of nonresponders in the absence of the signal ("false alarms" or false positives, i.e., nonresponders at a particular clozapine plasma concentration range). Receiver operating characteristic curves for the clozapine and total clozapine (clozapine plus norclozapine) data sets are presented in figures 1 and 2. For situations in which maximizing sensitivity (the probability of a response in subjects who have high clozapine plasma concentrations) and minimizing specificity (the probability of no response to clozapine at low clozapine plasma concentrations) are equally important, the optimal cutoff score occurs at the point of furthest displacement of the curve. Because false positives represent nonresponders to clozapine, sensitivity is of paramount importance. The cutoff score that maximizes sensitivity (at the expense of specificity) occurs where the distance from the vertical axis is minimized while the distance to the horizontal axis is maximized. As illustrated in figures 1 and 2, for clozapine alone, a plasma concentration of 350 ng/ml or more satisfies this criterion, while for total clozapine (clozapine plus norclozapine) a concentration of 450 ng/ml or more is acceptable.

Clozapine concentrations of at least 350 ng/ml defined a group of 11 patients that included seven (63.6%) of the 11 patients who responded to the drug. Similarly, total clozapine concentrations of at least 450 ng/ml defined a group of 11 patients that included seven (63.6%) of the 11 patients who responded to the drug. Thus, both drug concentration measurements produced the same degree of sensitivity. Additionally, both drug measurements were able to produce the same degree of specificity. Clozapine concentrations of less than 350 ng/ml and total concentrations of less than 450 ng/ml predicted nonresponse in 77.8% (14 of 18) of the patients. Chi-square analyses on these data found significant differences between the responders and nonresponders at these particular cutoff concentrations (χ^2=4.97, df=1, p=0.03).

DISCUSSION

Clozapine obviously represents a major advance in the treatment of schizophrenia. In this study we found that 37.9% of schizophrenic patients who had not responded to antipsychotics responded to clozapine. This figure is similar to the 30% rate found by Kane et al. in a 6-week double-blind study (1). Meltzer et al. (10) reported that 61% of treatment-resistant schizophrenic patients responded to clozapine when treated for up to 12 months, suggesting that a trial of 6 weeks may not be adequate. An alternative explanation for Meltzer et al.'s finding may be that initially the plasma concentrations were too low, and when the dose was increased later, the patients eventually responded. This explanation seems reasonable when it is recognized that our response rate was 63.6% for patients with plasma clozapine concentrations greater than 350 ng/ml.

The data revealed a significant relation between clozapine plasma concentrations and clinical response. The only other demographic or clinical characteristics that distinguished the responders from the nonresponders were baseline total BPRS score and baseline BPRS anergia factor score. The data in table 2 indicate that the two positive symptom factors and the anergia factor showed significantly greater decreases in the responders than in the nonresponders. Interestingly, the anergia factor was greater at baseline for the nonresponders and appeared to improve regardless of the clozapine concentrations.

Simpson and Cooper (11) found that two patients who developed grand mal seizures while taking clozapine had plasma concentrations of 1313 and 2194 ng/ml. Although these data do not suggest any upper limit of clozapine plasma concentrations for therapeutic response, the upper plasma concentration boundary will most likely be limited by adverse effects. One would expect that the neuroreceptors important to the desired antipsychotic effects will become saturated at some plasma concentration, making further increases of minimal benefit.

Use of clozapine plasma concentration as a predictor of schizophrenic patients' response to treatment appears quite advantageous, since its sensitivity was nearly 64% and its specificity was almost 78%. To confirm the legitimacy of clozapine plasma concentration as a predictor of response, future investigations should demonstrate that nonresponding patients with plasma concentrations of less than 350 ng/ml will benefit from increasing the drug dose to yield plasma concentrations above 350 ng/ml.

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Hidden Severe Psychiatric Morbidity in Sentenced Prisoners: An Australian Study[1]

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Objective: The aim of this survey was to estimate the prevalence of severe mental disorders in a representative sample of sentenced prisoners. Method: The subjects were selected as a random sample of sentenced prisoners in Melbourne's three metropolitan prisons. Interviews were conducted with 158 men and 31 women. Clinicians used the Structured Clinical Interview for DSM-III-R (SCID) to diagnose psychotic, affective, and substance use disorders. Results: Six prisoners (3%) received current diagnoses of psychotic disorders, and 23 (12%) were diagnosed as having current mood disorders, mainly major depression. A lifetime diagnosis of at least one mental disorder each was made for 82% of the respondents, and in 26% more than one lifetime disorder was diagnosed. Sixty-nine percent received lifetime diagnoses of dependence on or abuse of alcohol, other psychoactive substances, or a combination of these. Conclusions: These findings do not indicate a large-scale shift of deinstitutionalized psychotically ill people from mental hospitals to prisons. They do, however, highlight the diversion into the corrections system of substance-dependent people and the apparent pool of prisoners with largely untreated major depression.

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Systematic information on the prevalence and types of severe mental disorders in prisoners is scarce, although reports have appeared in Great Britain (1), North America (2), and Australia (3). Commentators have speculated that the prevalence of mental disorders has increased in the last 30 years among people detained in prisons, jails, and remand centers and that these institutions have become repositories for the severely mentally ill (4). This is thought to be the unintended consequence of deinstitutionalization and of the trend worldwide toward more stringent procedures for involuntary commitment to mental hospitals. Until recently, however, there has been little information from prisons, jails, or remand centers to support or refute these views (2, 5, 6). This debate has tended to overshadow other areas of concern about mental disorders among prisoners.

Studies of subjects incarcerated in prisons have traditionally shown low prevalences of severe psychotic and mood disorders but high prevalences of chronic psychological and social problems, alcohol and drug dependence, and mental handicap and epilepsy (1, 2). Higher rates of severe mental disorders have been found in people detained in jails in the United States (5, 6) and remand centers in the United Kingdom and Australia (7, 8). Jails and remand centers typically detain people before trial or for short sentences, and mentally ill detainees may be diverted to psychiatric facilities before conviction or imprisonment (6).

A small number of prison surveys have used standardized diagnostic instruments and representative sampling (1, 2, 9); three North American studies (2, 9) used the Diagnostic Interview Schedule (DIS) (10). These studies suggested that 10% to 15% of prison subjects have major *DSM-III-R* psychotic or mood disorders and need appropriate services. In addition, between 47% and 72% of the prisoners in the North American studies have been diagnosed as abusing or being dependent on alcohol and up to 60% as abusing illicit drugs (2, 9).

The aim of this survey was to estimate the prevalence of severe mental disorders, individually and in

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combination, in a representative sample of sentenced prisoners in Melbourne. We had the opportunity to contrast their psychiatric condition with that of homeless and disaffiliated people in inner Melbourne (11). The question of mental disorders in remandees was not addressed directly in this study.

METHOD

Diagnosis

"Severe mental disorder" was defined as a disorder that met the *DSM-III-R* criteria for schizophrenia, other psychotic disorders, major mood disorders, dysthymic disorder, or substance abuse or dependence (alcohol or other). In addition, we recorded indicators of organic mental disorder. Both lifetime and current (past month) diagnoses were included.

We used modules of the Structured Clinical Interview for DSM-III-R (SCID) (12) as the primary diagnostic tool, supplemented by the Mini-Mental State examination (13) as an indicator of cognitive impairment and extra questions on family and personal history. We had access to demographic and sentencing data from the Office of Corrections Victoria. The coordinator (J.M.) and the interviewers (two psychiatric nurses and a psychologist) had trained and used the instruments in a survey of homeless people in Melbourne (11). Two psychiatrists (H.H. and P.M.) made informal consensus diagnoses of organic mental disorder using information from the interviews and from discussions in regular supervision sessions.

Sampling Procedures

The subjects were selected as a random sample, stratified by sex and prison, of the sentenced prisoners who were held in late 1987 in the three Melbourne metropolitan prisons: Pentridge, Metropolitan Remand Prison, and Fairlea. Of the approximately 1,900 sentenced prisoners in Victoria in mid-1987, 800 men and 100 women were held in these prisons, and the remainder were in rural prisons. In general, those in rural prisons had been convicted of less serious crimes or were further along in their sentences than the metropolitan prisoners.

Prisoners in the prison psychiatric unit (capacity, 54) at the time of the survey were not included in the study sample. Information about them was collected separately, from unit records.

For each prison the Office of Corrections provided midnight census results for specified dates. The samples were chosen by means of a random number list. The interviewing in each prison took several weeks, and prisoners transferred or released before interview were replaced by other prisoners about to be moved.

A midnight census of male prisoners in Pentridge in late September 1987 yielded 408 names, and a second census 1 month later provided 134 additional names. A total sample of 140 men (a one-in-four sample) was selected from the study population of 542. Over 6 weeks in December and January, 43 further prisoners were selected for interview from lists of those due for release or due to be transferred to rural prisons. The researchers saw all prisoners eligible on a given day or, if all eligible prisoners could not be seen in 1 day, selected names ballot-style from a box.

At Metropolitan Remand Prison a sample of 94 men (a one-in-three sample) was selected from a census population of 300 in December 1987. A further 36 were selected to serve as replacements, from lists of those due for release or due to be transferred to rural prisons, by means of the procedures already described. A one-in-two sample of 44 women from Pentridge and Fairlea was selected in February 1988, and four women were selected later for replacement interviews.

The subjects who agreed to participate gave informed verbal consent to the interviews, which were conducted in private rooms. The information was used confidentially. For the prisoners who refused interview, we collected demographic and sentencing information from Office of Corrections files, data on previous use of psychiatric services from the Victoria Psychiatric Case Register, and other information from pre-sentence and other medical reports in the prison files.

Sample Characteristics

Of the 278 prisoners selected in the samples, 94 (34%) were transferred or released before interview and one died. Of the 183 prisoners approached for interviews, 136 agreed and 47 refused. An additional 68 potential replacements were asked to participate; 53 agreed and 15 refused. Therefore, a total of 189 were interviewed, 75% of those asked.

The interviewed subjects were predominantly young (32% were aged 15 to 24 years and 48% were 25 to 34) and male (158 men and 31 women; 84% and 16%, respectively). The profile for those refusing interview was similar: 51 (82%) were male and 11 were female, and 32% were 15 to 24 years old and 42% were 25 to 34. In the June 1987 Office of Corrections census of prisoners, 76% were younger than 35 years.

Previous terms of imprisonment had been served by 78% of the men (N=123) and 87% of the women (N=27). The comparable figures for the June 1987 census of prisoners were 73% for men and 65% for women. The median number of prior prison terms was two each for the original subjects chosen from the census lists, the replacement subjects, and the prisoners who refused interview.

The median time since entry into prison varied significantly across the original subjects, replacements, and refusers, according to Kruskal-Wallis nonparametric one-way analysis of variance ($\chi^2=25.47$, df=2, $p<0.0001$). According to Mann-Whitney U tests, the median time was significantly shorter in the replacements (85 days) than in either the original subjects (161 days; $z=-4.01$, $p=0.0001$) or the refusers (240 days; $z=-4.95$, $p<0.0001$) but did not differ significantly between the original subjects and the refusers ($z=-1.51$, $p=0.13$).

The median minimum sentence also varied significantly across the three groups ($\chi^2=6.51$, df=2, $p=0.04$). It was significantly shorter in the replacement subjects than in the original subjects (360 and 730 days, respectively; $z=-2.45$, $p=0.02$), but there was no significant difference between the refusers (542 days) and either the replacements ($z=-1.10$, $p=0.27$) or the original subjects ($z=-1.56$, $p=0.12$).

Among the 155 male respondents on whom we had relevant information, the most serious offense leading to the current imprisonment for 87 (56%) was a crime classified as violent (ranging from willful damage to murder but excluding sexual crimes). For 46 (30%) the most serious offense was a drug-related crime (including possession and trafficking), and for 16 (10%) it was a sex-related crime (ranging from indecent assault to aggravated rape). The proportions of prisoners in these categories of most serious offense did not differ significantly across the original subjects, replacements, and refusers.

RESULTS

The prevalence of disorders in the 189 interviewed subjects is shown in table 1. To the mood disorder category we assigned the major affective disorders, including major depression, mania, and dysthymia. The "psychotic" diagnoses include all other psychotic diagnoses.

Mood disorders, predominantly major depression, were the most common current diagnoses (12%). Six respondents were assigned current diagnoses of psychotic disorder. We did not systematically collect information on current substance use for ethical reasons.

Lifetime diagnoses of mood disorder were made in 34% of the subjects, psychotic disorder in 6%, and dependence on (predominantly) or abuse of alcohol and/or illicit substances in 69%. A lifetime diagnosis of at least one mental disorder each was made for 82% of the respondents, and in 26% more than one lifetime disorder was diagnosed (see table 2).

There were no significant associations between the minimum sentence length or time since entry into prison and a diagnosis of current mood disorder. Nor did we find an association between age and the prevalence of either lifetime or current disorders of any type.

Of the 53 replacements, seven (13%) received current diagnoses of mood disorder, 11 (20%) received lifetime diagnoses of mood disorder, and 37 (70%) were given lifetime diagnoses of substance use disorder. Ten (19%) had lifetime diagnoses in both of these categories, and one had lifetime diagnoses of both psychotic and substance use disorders. The pattern of disorders was similar to that in the overall sample.

TABLE 1. Major *DSM-III-R* Diagnoses Among 189 Sentenced Prisoners in Melbourne

	Lifetime		Current	
Disorder	N	%	N	%
Mood disorders	65	34	23	12
Bipolar disorder	1	1	0	0
Other bipolar disorder	6	3	2	1
Major depression	55	29	18	10
Dysthymia	0	0	3	2
Depressive disorder not otherwise specified	3	2	0	0
Psychotic disorders	11	6	6	3
Schizophrenia	6	3	4	2
Schizophreniform disorder	1	1	0	0
Psychotic disorder not otherwise specified	4	2	2	1
Substance use disorders	131	69	—[a]	—[a]
Alcohol abuse	8	4	—[a]	—[a]
Alcohol dependence	72	38	—[a]	—[a]
Other substance abuse[b]	38[c]	—	—[a]	—[a]
Other substance dependence[b]	185[d]	—	—[a]	—[a]

[a] Information on current substance use disorders was not collected systematically.

[b] More than one diagnosis may apply per subject, so N represents number of diagnoses. Other substance abuse was diagnosed in 32 subjects (17%), and other substance dependence was diagnosed in 98 subjects (52%).

[c] Sedatives, N=2; cannabis, N=25; stimulants, N=6; hallucinogens, N=4; multiple drugs, N=1.

[d] Sedatives, N=30; cannabis, N=29; stimulants, N=47; opioids, N=54; cocaine, N=4; hallucinogens, N=3; other, N=3; multiple drugs, N=15.

We reached informal consensus diagnoses of organic mental disorder for 16 subjects; most had organic affective and/or delusional disorders. All had concurrent diagnoses of substance-related disorders. Three subjects were probably mentally retarded (all three had other diagnoses).

Of the 62 prisoners who refused interview, two had probable current diagnoses, one of psychosis and one of mood disorder, and another two had probable lifetime diagnoses of mood disorder. Twelve (19%) had probable histories of alcohol abuse or dependence, and 28 (45%) had probable histories of abuse of or dependence on illicit psychoactive substances. This information suggests that their pattern of severe disorders was similar to that in the interviewed subjects.

In the prison psychiatric unit (not included in the census), 14 of the 38 inmates at the time of the census had probable lifetime diagnoses of psychotic disorder, and one had a probable lifetime diagnosis of major depression; six were currently psychotic. Alcohol (N=16) and illicit substance abuse or dependence (N=23) were the most common lifetime diagnoses. Five inmates evidently had organic mental disorder.

DISCUSSION

In this study, trained and supervised clinician interviewers used a standardized diagnostic instrument, a

TABLE 2. Categories of *DSM-III-R* Disorders in Male and Female Sentenced Prisoners in Melbourne

Disorder Category (mutually exclusive)	Lifetime[a]						Current[a]					
	Male (N=158)		Female (N=31)		Total (N=189)		Male (N=158)		Female (N=31)		Total (N=189)	
	N	%	N	%	N	%	N	%	N	%	N	%
One category												
Mood disorders	19	12	2	7	21	11	19	12	4	13	23	12
Psychotic disorders	0	0	0	0	0	0	3	2	3	10	6	3
Substance use disorders	74	47	11	36	85	45	—[b]	—[b]	—[b]	—[b]	—[b]	—[b]
Two categories												
Mood and substance	30	19	8	26	38	20	—[b]	—[b]	—[b]	—[b]	—[b]	—[b]
Mood and psychotic	1	1	2	7	3	2	0	0	0	0	0	0
Psychotic and substance	3	2	2	7	5	3	—[b]	—[b]	—[b]	—[b]	—[b]	—[b]
All three categories	3	2	0	0	3	2	—[b]	—[b]	—[b]	—[b]	—[b]	—[b]
No disorders	28	18	6	19	34	18	136	86	24	77	160	85

[a] Lifetime diagnoses include current diagnoses (except dysthymia), but an individual with a current diagnosis in one category may have lifetime diagnoses in one or two other categories.
[b] Information on current substance use disorders was not collected systematically.

procedure unusual in other studies of this type, to define a range of severe mental disorders in a representative group of sentenced prisoners. The replacements, as expected, had overall shorter stays than the other subjects. Comparisons of the interviewed subjects and the prisoners who refused interview failed to indicate major systematic differences on a number of variables.

The high prevalences of substance dependence and major mood disorders are consistent with findings from other studies, although we did not find the high rate of dysthymic disorder noted in the DIS surveys (2, 9). This difference may be due to the clinicians' use of the less structured SCID, which allows probing of responses and consideration of context in judging the presence or absence of symptoms. Psychotic disorders were relatively uncommon, and the prevalence is likely to be unreliable in a sample of this size.

Nonetheless, the survey gives an indication of the scale of the problem, and our findings are consistent with those from the North American surveys. Information obtained about prisoners who refused interview and separate analysis of the replacement sample both suggest that we did not miss large numbers of prisoners with psychotic disorders.

We did not consider mental retardation and personality disorders, and our ability to diagnose organic mental disorder was limited because we did not perform physical examinations.

We were unable to confirm a large-scale shift of deinstitutionalized psychotically ill people from mental hospitals to prisons and did not find a large pool of hidden morbidity from psychotic disorders. These findings contrast with the high rate of psychotic disorders found in homeless and disaffiliated people in inner Melbourne in the winter of 1987 (11). We do not, however, dismiss the implications of the possibility that 30 to 40 people with current psychotic disorders are serving sentences in the Melbourne metropolitan prisons at any one time. This includes a number who are receiving treatment in the prison psychiatric unit. It is also likely that a number of people with psychotic disorders who are in remand centers are diverted to psychiatric services before sentencing or, if sentenced, are given short terms of imprisonment. Two other issues are important to the public health in both Australia and North America: the diversion into the corrections system of substance-dependent people and the apparent pool of prisoners with largely untreated major depression.

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Characteristics of Psychotic Inpatients With High or Low HVA Levels at Admission

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Objective: The purpose of this study was to examine the clinical profiles of psychotic patients whose fasting levels of plasma free homovanillic acid (HVA) were elevated on the day after admission to the hospital. Method: These 85 subjects with nonorganic psychoses had been previously studied with respect to their response to neuroleptic treatment. They were divided into two groups on the basis of a median split of their pretreatment plasma HVA levels, and the two groups were compared on a number of clinical and demographic variables ascertained during their hospital stay. Fasting levels of plasma free HVA and 3-methoxy-4-hydroxyphenylglycol (MHPG) were measured by gas chromatography-mass spectrometry. Results: The high-HVA group tended to show a better prognostic profile than the low-HVA group; however, the only significant difference between groups was in the greater use of psychotogenic drugs by low-HVA males. Fourteen additional psychotic patients with distinctly elevated HVA levels and normal MHPG values were also diagnostically heterogeneous. Conclusions: The results suggest that psychotic patients with different diagnoses who have relatively high levels of plasma free HVA before treatment will show a favorable early response to neuroleptic drugs. There may be neurobiological processes linking some patients across the clinical spectrum of the psychotic disorders.

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There have been many efforts in the past few years to characterize the nonorganic psychotic conditions with respect to nosology and family history (1, 2). Biologically defined categories have only begun to appear (3). My colleagues and I previously reported that pretreatment levels of plasma free homovanillic acid (HVA), a metabolite of dopamine, and to some extent 3-methoxy-4-hydroxyphenylglycol (MHPG), a metabolite of norepinephrine, were significantly elevated before neuroleptic treatment in a group of acute psychotic patients of varying diagnoses who had a relatively favorable early response (10 days) to a modest neuroleptic dose (4–7). The actual correlation between pretreatment level of plasma HVA and early response in our studies has not usually been greater than 0.50, because some patients with normal pretreatment HVA values have also had a good response. However, in our experience a pretreatment plasma HVA level of 18 ng/ml or more is virtually always associated with a favorable early neuroleptic response. This finding suggests the possibility of a biochemically defined clinical subgroup among the psychoses that has a significant clinical correlate (favorable early neuroleptic response). In an effort to pursue other clinical factors possibly associated with elevated pretreatment levels of plasma HVA in acute psychotic states, my associates and I performed a median split according to the pretreatment levels of plasma HVA in our subjects whose early treatment response had previously been determined and then compared the characteristics of the two groups.

METHOD

Eighty-five consecutively admitted inpatients with nonorganic psychoses who gave informed consent were studied: 45 males aged 15–55 years and 40 females aged 16–65 years. All had been previously involved in prospective neuroleptic trials to determine early (10-day) neuroleptic response. The details of these studies have been described elsewhere (4–7). In brief, the patients had been given diagnoses according to *DSM-III* criteria on the basis of all available clinical

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TABLE 1. Data on Psychotic Inpatients Grouped According to Median Plasma HVA Levels at Admission—Continuous Variables

	Males				Females			
	High HVA (N=23)		Low HVA (N=22)		High HVA (N=20)		Low HVA (N=20)	
Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD
HVA level (ng/ml)	18.6	3.6	11.1	2.2	22.5	8.4	11.6	2.1
MHPG level (ng/ml)[a]	4.1	1.4	4.2	1.3	4.3	1.4	4.0	1.3
Age (years)	26.8	8.6	23.8	9.0	31.8	9.3	30.4	13.1
Age at onset (years)	25.2[b]	6.8	21.7[b]	6.2	27.3	8.8	26.3	11.7
Number of hospitalizations	1.4	1.0	1.4	0.7	2.0	2.0	2.1	1.4
Duration of illness prior to current hospitalization (weeks)	9.3	9.9	6.4	7.2	9.3	11.0	6.4	5.3
BPRS score								
Depression	3.7	2.4	3.1	2.1	4.0	2.0	4.0	2.2
Guilt	3.2	2.9	2.4	2.1	2.4	2.6	3.0	2.3
Mania	2.0	2.4	3.1	2.9	2.8	2.8	3.1	3.2
Paranoia	6.0	1.5	6.0	1.8	6.1	1.8	6.0	1.6
Psychomotor retardation	1.6	2.5	2.0	3.1	1.6[c]	2.0	2.8[c]	2.8

[a] N=20 for high-HVA males, N=18 for low-HVA males, N=19 for high-HVA females, and N=16 for low-HVA females.

[b] Trend toward significant difference between high-HVA and low-HVA males (t=1.8, df=43, p=0.08).

[c] Trend toward significant difference between high-HVA and low-HVA females (t=1.6, df=38, p=0.10).

material. None had received more than 5 mg of haloperidol or its equivalent for at least 1 week before admission. Fasting levels of plasma free HVA and MHPG were determined on the morning after admission. The neuroleptic trials included a variable-dose haloperidol group (serum level measured) (4), a fixed-dose haloperidol group (0.2 mg/kg per day) (6), and a fixed-dose perphenazine group (0.5 mg/kg per day) (7). Response was assessed on the 10th day by independent raters using the Brief Psychiatric Rating Scale (BPRS) and a global assessment of residual psychotic symptoms (7). In each study pretreatment fasting levels of plasma free HVA were significantly correlated (Pearson r) with early neuroleptic response. For the total group the correlation between HVA level and response was 0.46 (N=85, $p<0.001$) and between MHPG level and response, 0.30 (N=73, $p<0.01$). The correlation between HVA and MHPG levels was also 0.30 (N=73, $p<0.01$). HVA and MHPG levels were not significantly correlated with age.

Having identified a subgroup of subjects in whom pretreatment HVA levels were related to neuroleptic response, we performed a median split of the pretreatment HVA values, forming a high-HVA group (N=43) and a low-HVA group (N=42). We then compared these two groups by sex on the following items: age, marital status, HVA and MHPG levels, diagnosis, number of previous hospitalizations, age at onset of psychotic symptoms, duration of psychotic symptoms in the current episode, schizoid-asocial development (Gittelman-Klein scale) (8), psychotogenic drug use (primarily marijuana and/or cocaine), family history (first- or second-degree relative hospitalized for a psychiatric disorder other than alcoholism), and current symptoms, including the BPRS items for depressed mood, guilt, excitement, suspiciousness, psychomotor retardation, and auditory hallucinations. Suicidal ideation or act was also scored. Details of these assessments, including interrater agreement, have been previously published (9).

In a further effort to maximize the specificity of elevated plasma HVA values, we collected data on another group of 14 psychotic patients who had been admitted to the inpatient service over a 3-year period and were characterized by pretreatment HVA values of 22 ng/ml or more and MHPG values of less than 5 ng/ml, i.e., distinctly elevated HVA levels and normal MHPG levels. Their fasting levels of plasma free HVA and MHPG were measured by gas chromatography and mass spectrometry as previously described (4). Dichotomous variables were compared by chi-square with Yates' correction, and continuous variables were compared by t test (two-tailed).

RESULTS

Table 1 presents descriptive data for males and females divided into high- and low-HVA groups. The high- and low-HVA groups for both males and females did not differ with respect to MHPG level, nor did the two groups differ with regard to age for either sex. Diagnoses also were not different for the high- and low-HVA groups. The number of patients hospitalized for the first time was approximately the same for the two groups for both sexes.

Table 1 also shows the results obtained when the continuous clinical variables for the high- and low-HVA groups were compared. No differences were significant at the 0.05 level. Two possible trends were noted: males in the high-HVA group tended to be older at onset, and females in the low-HVA group tended to show more psychomotor retardation.

Table 2 shows the results for the dichotomous clin-

TABLE 2. Data on Psychotic Inpatients Grouped According to Median Plasma HVA Levels at Admission—Dichotomous Variables

	Males				Females			
	High HVA (N=23)		Low HVA (N=22)		High HVA (N=20)		Low HVA (N=20)	
Variable	N	%	N	%	N	%	N	%
Diagnosis								
Schizophrenia	3	13.0	2	9.1	4	20.0	3	15.0
Schizophreniform disorder	6	26.1	3	13.6	2	10.0	1	5.0
Schizoaffective disorder	2	8.7	4	18.2	4	20.0	3	15.0
Atypical psychosis	5	21.7	4	18.2	1	5.0	5	25.0
Mania, psychosis	3	13.0	8	36.4	6	30.0	5	25.0
Depression, psychosis	3	13.0	1	4.5	3	15.0	2	10.0
Paranoid disorder	1	4.3	0	0.0	0	0.0	1	5.0
First hospitalization	17	73.9	16	72.7	10	50.0	11	55.0
Ever married	8	34.8[a]	3	13.6[a]	9	45.0	9	45.0
Schizoid history	9	39.1	5	22.7	4	20.0	6	30.0
Auditory hallucinations	14	60.9	11	50.0	10	50.0[b]	15	75.0[b]
Drug use	5	21.7[c]	15	68.2[c]	5	25.0	8	40.0
Family history of psychiatric disorder	11	47.8	14	63.6	12	60.0	12	60.0
Suicidal	8	34.8	7	31.8	3	15.0	6	30.0

[a] Trend toward significant difference between high-HVA and low-HVA males ($\chi^2=2.9$, df=1, p=0.09).

[b] Trend toward significant difference between high-HVA and low-HVA females ($\chi^2=2.7$, df=1, p=0.10).

[c] Significant difference between high-HVA and low-HVA males ($\chi^2=10.0$, df=1, p=0.002).

TABLE 3. Data on 14 Additional Psychotic Inpatients With HVA Levels Greater Than 22 ng/ml and MHPG Levels Less Than 5 ng/ml

Patient	Sex	Age (years)[a]	Diagnosis	HVA Level (ng/ml)[b]	MHPG Level (ng/ml)[c]
1	F	21	Major depression, psychosis	34.1	4.6
2	F	26	Major depression, psychosis	30.7	2.9
3	F	47	Major depression, psychosis	32.2	3.8
4	F	14	Mania, psychosis	24.2	4.4
5	F	36	Mania, psychosis	31.0	3.3
6	M	19	Schizoaffective disorder	22.0	3.1
7	F	18	Brief reactive psychosis	29.7	2.9
8	F	21	Atypical psychosis	27.2	4.6
9	F	35	Atypical psychosis	32.4	4.4
10	F	50	Atypical psychosis	29.3	3.9
11	M	41	Paranoid disorder	27.2	3.4
12	F	24	Schizophrenia	32.0	3.4
13	F	24	Schizophrenia	24.9	2.2
14	M	23	Schizophrenia	23.4	3.5

[a] Mean±SD=28.5±11.3 years.

[b] Mean+SD=28.5±3.8 ng/ml.

[c] Mean+SD=3.6±0.7 ng/ml.

ical variables. The only significant difference was in drug use by males; the low-HVA males clearly were more likely to have used psychotogenic drugs to a significant extent. There was a trend for a higher proportion of high-HVA males than low-HVA males to have been married and for a greater proportion of low-HVA females than high-HVA females to have auditory hallucinations. Family history was not different between the two groups for either sex.

Data on the supplementary cases chosen for elevated HVA values alone also indicated a diagnostically heterogeneous group (table 3). Six patients were diagnosed as having affective psychoses, three were diagnosed as having schizophrenia, and the balance had other nonaffective psychoses. There were 11 females and 3 males.

DISCUSSION

The high- and low-HVA groups formed by a median split of pretreatment, fasting levels of plasma free HVA in newly admitted psychotic patients did not show many clinical differences. The major clinical characteristic of the patients with elevated levels of plasma HVA was a relatively good early neuroleptic response, which had been previously assessed in separate studies. Other differences that emerged in the group comparisons tended to indicate a somewhat better prognostic profile for the high-HVA subjects. High-HVA males tended to have been older at onset and to have been married at some period in their lives. High-HVA females tended to have auditory hallucinations less often and to show less psychomotor retardation.

The major group difference was in the degree of previous psychotogenic drug use by the high- and low-HVA males. This was an unanticipated finding, and its meaning is unclear. We cannot assume from our data that there was a relation between plasma HVA values and psychotogenic drug use, but the findings are consistent with this possibility. Since all of our patients had been admitted for a first or second episode, differences in chronicity of illness could not account for these findings (10, 11). It is possible that periodic psychotogenic drug use could affect dopaminergic neuronal systems and be reflected in plasma HVA levels. My colleagues and I pursued this matter in another study that focused on early neuroleptic response and the significance of previous psychotogenic drug use (12).

It is noteworthy that there was no difference in duration of illness prior to hospitalization for the groups of either sex. Elevated levels of plasma HVA might have been hypothesized as resulting from an acute response to stress, most likely associated with psychotic disorders of recent onset. However, the finding that the high-HVA groups had, if anything, a somewhat longer duration of illness does not support that possibility. It is also clear that having a first- or second-degree family member who had been hospitalized for psychiatric illness did not distinguish the high- and low-HVA groups, so that at this relatively inexact level of family diagnosis, at least, there is no evidence that the high-HVA characteristic has a genetic origin.

It is apparent from our data that an elevated pretreatment level of plasma HVA is not necessarily likely to be associated with good long-term prognosis but only with a favorable early neuroleptic response. For example, 20%–40% of the high-HVA group had a schizoid developmental history, a factor that is usually associated with a relatively poor social prognosis. It is quite likely that neuroleptic response, like other factors contributing to long-term outcome, is not highly intercorrelated with these other factors.

If an elevated pretreatment level of plasma HVA and its correlate of favorable early neuroleptic response suggest a neurochemically defined subgroup, then it appears that this subgroup cuts across current descriptive nosological categories. Our findings may relate to the report of Kendler et al. (1) on their family study of nonschizophrenic psychotic disorders. They showed that there is a greater prevalence of a variety of psychotic disorders, including schizophrenia, among the family members of probands with psychotic affective disorders. Thus, there may be neurobiological processes linking some patients across the spectrum of the psychotic disorders.

Our results suggest that there are patients with a variety of diagnoses of nonorganic psychoses who are characterized by a relatively high level of plasma free HVA while they are psychotic and before treatment and who will show a favorable early response to modest doses of neuroleptic drugs. These patients may constitute a true subgroup, based on etiology or some other fundamental common characteristic, or they may simply be a group of patients with similar early responses to treatment and a common marker for that treatment. In either case, plasma HVA level should be investigated further as a clinically relevant measure in patients with nonorganic psychoses of recent onset.

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Cold Agglutinin Autoantibodies in Psychiatric Patients: Their Relation to Diagnosis and Pharmacological Treatment

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Background and Method: The purpose of this study was to compare titers of cold agglutinins in schizophrenic patients with those in patients with major affective disorders and in normal healthy subjects. One hundred sixty-six psychiatric patients and 37 healthy comparison subjects were included in the study. Ninety of the patients suffered from schizophrenia, 54 from bipolar disorder, and 22 from major depression. Venous blood samples were obtained from all subjects between 8:00 and 10:00 a.m. and were immediately tested for cold agglutinin titers. Results: A high frequency (42.2%) of positive cold agglutinin titers was detected in the schizophrenic patients, compared with the bipolar (11.1%) and unipolar (9.0%) patients and the comparison group (8.1%). The investigators did not find any pharmacological effect on these results. Conclusions: The findings suggest that, at least in this group, positive cold agglutinin titers are associated with schizophrenia. However, this observation cannot provide direct evidence for the involvement of viral or autoimmune factors in schizophrenia.

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Cold agglutinins are usually autoantibodies of the IgM class. IgA, IgG, and mixed IgM-IgG cold agglutinins have also been found (1). They are most often directed against the I antigen or related antigens on red blood cells. However, cold agglutinins specific to antigens on monocytes, macrophages, platelets, and T and B lymphocytes have been shown (1, 2). High titers of polyclonal cold agglutinins are usually associated with infection, particularly mycoplasmal pneumonia, syphilis, viral infections (especially respiratory), infectious mononucleosis, cytomegalovirus infections, mumps (1–3), infectious hepatitis, rubella (4), and secondary cold urticaria (5). They are detected in disorders associated with autoantibody production, such as systemic lupus erythematosus, rheumatoid arthritis, thyroid autoimmune disorders, ulcerative colitis, and chronic active hepatitis (2, 3). Most monoclonal cold agglutinins are found in patients with lymphoreticular neoplasms (2) and chronic cold hemagglutinin disease (3). In a previous study we found that schizophrenic patients tended to have positive cold agglutinin titers (6). This finding can indicate a response of the humoral immune system to an autoimmune process, a viral infection, or a response to long-term neuroleptic treatment, as was suggested previously for other immunological alterations reported in schizophrenia (6–9).

To further clarify these interpretations, we assessed cold agglutinin titers in a large group of psychiatric patients, with special attention to the effect of pharmacological treatment.

METHOD

One hundred sixty-six psychiatric patients and 37 comparison subjects were included in the study. Of the 166 patients, 90 were diagnosed as having schizophrenia (chronic, disorganized type), 54 had a diagnosis of bipolar disorder, and 22 had a diagnosis of major depression. Of the schizophrenic patients, 37 had been drug free for at least 3 months before testing, 33 had been treated with haloperidol for at least 3 months before testing (mean±SD dose=28±17 mg/day), and 20 had never received psychotropic medication. Of the bipolar patients, 20 had been drug free for at least 3 months before testing, and 34 had been maintained on a regimen of lithium carbonate for at least 3 months (mean±SD dose of lithium carbonate=854±241 mg/day; mean±SD serum level of lithium=0.5±0.3 meq/liter).

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TABLE 1. Demographic and Cold Agglutinins Data of 166 Psychiatric Patients and 37 Healthy Comparison Subjects

Group	Age (years)		Sex		Cold Agglutinin Titration Test Results			
	Mean	SD	M	F	Total Negative	Total Positive	Positive at 1:2	Positive at 1:4
Chronic schizophrenia								
≥3 months drug free (N=37)	38.9	11.5	21	16	21	16	10	6
≥3 months haloperidol treatment (N=33)	36.6	10.7	16	17	19	14	5	9
Never treated (N=20)	28.1	7.2	10	10	12	8	5	3
Bipolar disorder								
≥3 months drug free (N=20)	37.7	12.5	7	13	19	1	1	0
≥3 months lithium treatment (N=34)	44.7[a]	12.4	17	17	29	5	3	2
Major depression, ≥3 months drug free (N=22)	46.9[b]	10.9	10	12	20	2	2	2
Healthy comparison subjects (N=37)	41.1[c]	14.1	20	17	34	3	2	1

[a] Significantly different from the schizophrenic patients who had been drug free for at least 3 months (F=4.14, df=6, 196, p=0.0006).
[b] Significantly different from the schizophrenic patients who had never been treated (F=4.41, df=6, 196, p=0.0003).
[c] Significantly different from the schizophrenic patients who had been drug free for at least 3 months (F=2.63, df=6, 196, p=0.02).

All patients were in good physical condition and not addicted (had no current or past diagnoses of substance abuse or dependence). Diagnoses were established according to *DSM-III-R* criteria by using detailed information obtained from structured interviews according to the guidelines of the Schedule for Affective Disorders and Schizophrenia—Lifetime Version (10), medical records, and interviews of family members. Full consensus between two senior psychiatrists was required for final diagnosis. The chronic, disorganized schizophrenic patients were in acute exacerbation requiring admission, the lithium-treated bipolar patients were euthymic, and the untreated bipolar patients were admitted during a manic episode. The unipolar patients were admitted during an episode of major depression. The comparison subjects, healthy medical staff volunteers, were interviewed by a psychiatrist (B.S.), and there was no evidence of current or lifetime mental disorder. Informed consent was obtained from each patient and comparison subject. All subjects underwent physical examinations and had the SMA-12 series of routine blood tests and a CBC in order to exclude any pathological physical condition (especially, recent febrile or infectious illness) at the time of the study. Venous blood samples were obtained from the patients and the comparison subjects at 8:00–10:00 a.m. and were immediately tested for cold agglutinin titers according to the cold agglutinin titration method (10). The measures were carried out blindly. The reliability of the method for cold agglutinin titration testing in our laboratory is approximately 95%.

The data were analyzed by Fisher's exact test, two-tailed, for intergroup comparisons. The two-tailed Student's t test was used to determine the influence of age, haloperidol dosage, lithium dosage, and lithium serum level on the cold agglutinin test titers. Additionally, the data were analyzed by chi-square test to determine the influence of sex. One-way analysis of variance and the chi-square test were used to compare age and sex distribution among the comparison subjects and the patients.

RESULTS

The demographic and cold agglutinin data of the patients and comparison subjects are summarized in table 1. The group of patients with major depression was significantly older than the group of schizophrenic patients who had never received psychotropic medication. The group of bipolar patients treated with lithium carbonate was also significantly older than the group of drug-free schizophrenic patients. The comparison group was significantly older than the group of schizophrenic patients who had been drug free for at least 3 months. There was no significant difference between the subject groups with respect to sex (χ^2=2.93, df=6, p=0.18).

The titers of the patients and the comparison subjects who had positive cold agglutinin tests did not exceed 1:4 (table 1). Significantly more schizophrenic patients than comparison subjects and unipolar and bipolar affective patients had positive test results (table 2). There was no significant difference in positive test results among the subgroups of schizophrenic patients: those treated with haloperidol, those who had been drug free for at least 3 months, and those who had never received psychotropic medication In addition, no significant difference was found among the bipolar disorder patients treated with lithium carbonate, the patients with unipolar major depression, the bipolar patients who had been drug free for at least 3 months, and the comparison subjects. The statistical results of

TABLE 2. Statistical Differences in Cold Agglutinin Titers Between 166 Psychiatric Patients and 37 Healthy Comparison Subjects

	p Value (Fisher's exact test, two-tailed)					
	Chronic Schizophrenia			Bipolar Disorder		Major Depression (≥3 Months Drug Free)
Group	≥3 Months Drug Free	≥3 Months Haloperidol Treatment	Never Treated	≥3 Months Drug Free	≥3 Months Lithium Treatment	
Chronic schizophrenia						
≥3 months drug free (N=37)	—	—	—	—	—	—
≥3 months haloperidol treatment (N=33)	0.86	—	—	—	—	—
Never treated (N=20)	0.96	0.91	—	—	—	—
Bipolar disorder						
≥3 months drug free (N=20)	0.004	0.006	0.02	—	—	—
≥3 months lithium treatment (N=34)	0.02	0.02	0.08	0.54	—	—
Major depression, ≥3 months drug free (N=22)	0.01	0.01	0.04	0.93	0.86	—
Healthy comparison subjects (N=37)	0.002	0.002	0.01	0.88	0.62	0.60

TABLE 3. Statistical Differences in Cold Agglutinin Titers Between 166 Psychiatric Patients and 37 Healthy Comparison Subjects Without Reference to Pharmacological Treatment

	p Value (Fisher's exact test, two-tailed)		
Group	All Schizophrenic Patients	All Bipolar Patients	Major Depressive Patients
All schizophrenic patients (N=90)	—	—	—
All bipolar patients (N=54)	<0.0001	—	—
Major depressive patients (N=22)	0.004	0.84	—
Healthy comparison subjects (N=37)	<0.0001	0.92	0.53

the comparisons between groups are shown in table 2. Since there was no statistical evidence suggesting an effect of haloperidol and/or lithium on the positive cold agglutinin titers, we pooled all the schizophrenic patients, treated and untreated (N=90), and compared them to all the bipolar patients (N=54), patients with unipolar major depression (N=22), and the comparison subjects (N=37). Significantly more schizophrenic patients had positive test results than did the other groups (table 3). We did not find a significant difference in positive test results among the comparison subjects and bipolar and unipolar affective patients (table 3).

There were no significant differences between patients with positive cold agglutinin test results and those with negative results in age, sex, dose of haloperidol in haloperidol-treated chronic schizophrenic patients, and dose of lithium carbonate and lithium serum levels in lithium-treated bipolar patients (table 4).

TABLE 4. Statistical Differences in Age, Sex, and Drug Treatment Between Psychiatric Patients With Positive (N=46) and Negative (N=120) Cold Agglutinin Titers

Variable	Statistical Comparison
Age	t=0.54, df=201, p=0.59
Sex	χ^2=0.02, df=1, p=0.99
Dose of haloperidol	t=0.20, df=31, p=0.44
Dose of lithium	t=0.06, df=32, p=0.57
Lithium blood level	t=1.30, df=32, p=0.20

DISCUSSION

In this study we found a significantly higher frequency of positive cold agglutinin titers in the schizophrenic patients (42.2%) than in the bipolar (11.1%) and unipolar (9.0%) major affective patients and the comparison subjects (8.1%). We did not find any pharmacological effect on these results, contrary to our prior assumption (6). In our sample, age and sex did not affect the frequency of positive cold agglutinin titers. As all the subjects were in good physical condition, we cannot attribute this finding to any physical disorder. Our findings suggest that, at least in our sample, positive cold agglutinin titers are associated with schizophrenia. However, titers up to 1:4, such as were found in our patients, are not considered to be evidence of pathology (11) and can be found in healthy populations, too (12). The humoral immunological alteration observed in the schizophrenic patients we studied was not expressed by abnormal, elevated titers of cold agglutinins but by the presence of positive titers in about two-fifths of these patients. The prevalence of positive cold agglutinin titers in the healthy population is unknown (4). It is presumably similar to that of other autoantibodies from the same IgM class, which in the age range of our sample is about 4% (13)—

much smaller than the finding in our sample of schizophrenic patients (42.2%).

Although a positive cold agglutinin test result is a nonspecific humoral immunological response, it is possible that some schizophrenic patients with positive cold agglutinin titers are undergoing some autoimmune process or viral infection which is undetectable in routine physical and laboratory tests. The disturbances in the humoral immune system that we observed in our schizophrenic patients may be attributable to such a viral infection or autoimmune process (14, 15). The greater number of schizophrenic patients born in late winter or early spring could indicate prenatal exposure to a seasonal viral infection (16). Chronic schizophrenia is associated with an enlargement of the brain ventricles (17) and with paraventricular fibrillary gliosis (18), structural and histological changes that can occur following prenatal and postnatal viral infections (19).

Our observations cannot provide direct evidence that viral or autoimmune factors are implicated in schizophrenia. However, such a lack of direct evidence, mainly at the structural and morphological levels, is already known in medicine, mainly in viral and autoimmune diseases accompanied by psychiatric symptoms. One of the possible explanations for this discrepancy is the ability of viral infections and autoimmune processes to interfere with the molecular functioning of neurotransmission in the CNS without causing substantial histological changes (20–23). Even in an autoimmune neurotransmission disease such as myasthenia gravis, cholinergic dysfunction caused by specific antibodies is not expressed in substantial changes in abnormal tissue (24). The search for specific autoantibodies against components of CNS and/or viral factors that can interfere with neurotransmission in schizophrenic patients seems justified. Identifying a possible specific subtype of cold agglutinins associated with some schizophrenic patients, or identifying specific subsets of schizophrenic patients who have positive cold agglutinin titers, could clarify the relationship and interaction between the immune system and the pathophysiology of schizophrenia.

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Olfactory Identification Deficits in HIV Infection

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Objective: Impaired odor identification is described in a number of CNS disorders, and human immunodeficiency virus (HIV) infects the CNS in a large percentage of patients. To evaluate whether impaired olfaction may indicate CNS disease, the authors measured odor identification in patient groups defined along a continuum of progressive immunodeficiency and in a comparison group. Method: Most of the 42 HIV-infected patients in the study were outpatients in a clinic specializing in treatment of HIV-infected individuals. The comparison subjects were 37 healthy age- and sex-matched individuals who were recruited from hospital and medical school personnel. Ten of the patients were HIV-seropositive but had no symptoms, 24 had clinical evidence of immunocompromise, and eight had HIV dementia. All subjects were given the University of Pennsylvania Smell Identification Test, which presents common odorants and requires the subject to identify the odor from a four-item word list. The data were analyzed by using analysis of variance after arc-sine transformation and Scheffé post hoc analysis. Results: All patients scored significantly lower on the Smell Identification Test than did the comparison subjects. The patients with HIV dementia had significantly lower scores than did the other two groups of patients. Conclusions: Clinically, impaired olfaction might serve as a marker of early CNS HIV involvement. Future studies should attempt to match comparison and experimental populations for socioeconomic status and HIV risk behavior.

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Impaired odor identification is described in a number of CNS disorders, including Alzheimer's disease, Down's syndrome, and parkinsonian dementia. Olfactory deficits may be noted early in the clinical course of these diseases (1, 2).

The human immunodeficiency virus (HIV) infects the CNS in a large percentage of patients. In their series, Marshall et al. (3) described CSF abnormalities in approximately 60% of asymptomatic HIV-seropositive individuals. Neuropsychological abnormalities have been described in patients with AIDS-related complex and AIDS with no other presumed neurological risk. HIV dementia may occur in up to 40% of patients with AIDS. Brain pathology of HIV dementia reveals cell loss, inflammation, and other degenerative change (4).

Given evidence that impaired olfaction may indicate CNS disease, we measured odor identification in three patient groups—asymptomatic patients who were HIV-seropositive, patients with clinical evidence of immunocompromise, and patients with HIV dementia—and in a comparison group.

METHOD

After obtaining the patients' informed consent, we gave the University of Pennsylvania Smell Identification Test (5) to 42 HIV-infected patients. Ten of these patients were HIV-seropositive but had no symptoms, 24 had clinical evidence of immunocompromise, and eight had HIV dementia. With the exception of four patients with HIV dementia, the subjects were outpatients in a clinic specializing in treatment of HIV-infected individuals. The Smell Identification Test is a standardized, 40-item, microencapsulated, scratch-and-sniff odor identification instrument that presents common odorants and requires the subject to identify the odor from a four-item word list. With the excep-

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tion of four of the patients with HIV dementia, all patients were tested in the clinic. In most cases, the Smell Identification Test was given after the patient was asked a few demographic questions. All subjects were screened by using a standard list of exclusion criteria (6, 7) before olfactory testing.

The patient groups were defined along a continuum of progressive immunodeficiency. The asymptomatic HIV-seropositive patients had positive HIV antibody tests (ELISA, confirmed by Western blot) but were otherwise physically well and were not taking any medication. The patients with clinical evidence of immunocompromise had positive HIV antibody tests and had signs of immunodeficiency such as persistent generalized lymphadenopathy and T-lymphocyte counts of less than 200. Some of these patients did not meet Centers for Disease Control (CDC) criteria for AIDS; some did but had no psychiatric or neurological complaints and no evidence of dementia on routine clinical examination in an infectious disease clinic. Most patients in this group were taking zidovudine. The group of patients with HIV dementia included those who after complete neuropsychiatric evaluation were felt to have an HIV-related encephalopathy (e.g., their head CT showed atrophy without mass or they had nonspecific CSF changes).

The Smell Identification Test was also given to 37 healthy age- and sex-matched comparison subjects who were recruited from hospital and medical school personnel. The frequency of occurrence of HIV seropositivity in this comparison group is unknown but is presumed to be equal to that of the general population. We are not aware of any data suggesting that the frequency of occurrence of HIV seropositivity in hospital workers is different from that of the general population.

There were no statistically significant differences in mean±SD age among the four groups of subjects: asymptomatic HIV-seropositive patients, 36±7.1 years; patients with clinical evidence of immunocompromise, 35±8.1; patients with HIV dementia, 40±7.6; and comparison subjects, 37±7.8. Thirty-nine of the 42 patients were men. One asymptomatic HIV-seropositive subject had a remote history of coma secondary to an automobile accident. Groups were not matched for smoking history.

The data were analyzed by using analysis of variance (ANOVA) with arc-sine transformation and the Scheffé post hoc analysis (8); p<0.05 was considered significant.

RESULTS

There was a highly significant difference among the patient groups in Smell Identification Test scores (see table 1). All patient groups scored statistically significantly lower than did the comparison subjects. The patients with HIV dementia had statistically significantly lower Smell Identification Test scores than the asymptomatic patients who were HIV-seropositive and the patients with clinical evidence of immunocompromise. There was no statistically significant difference in test scores between the asymptomatic patients who were HIV-seropositive and the patients with clinical evidence of immunocompromise. The results were unchanged when the asymptomatic HIV-seropositive patient with a history of coma was excluded from the analysis.

TABLE 1. University of Pennsylvania Smell Identification Test Scores of HIV-Infected Patients and an Age- and Sex-Matched Normal Comparison Group

	Test Score[b]		
Group[a]	Mean	SD	Range
Normal comparison subjects (N=37)[c]	38.3	1.8	33–40
Asymptomatic HIV-seropositive patients (N=10)[d]	34.9	5.1	27–39
Patients with clinical evidence of immunocompromise (N=24)[e]	34.6	4.5	25–40
Patients with HIV dementia (N=8)	28.1	5.1	18–33

[a] Significant difference among groups (F=18.87, df=3, 75, p<0.0001).

[b] Highest possible score=40.

[c] Significantly different from asymptomatic HIV-seropositive patients (p<0.05), patients with clinical evidence of immunocompromise (p<0.01), and patients with HIV dementia (p<0.01) (Scheffé post hoc comparisons).

[d] Not significantly different from patients with clinical evidence of immunocompromise, significantly different from patients with HIV dementia (p<0.05) (Scheffé post hoc comparisons).

[e] Significantly different from patients with HIV dementia (p<0.01, Scheffé post hoc comparison).

DISCUSSION

This study demonstrates small but statistically significant differences in olfactory performance among patients at different stages of HIV infection. The difference in Smell Identification Test scores between comparison subjects and asymptomatic HIV-seropositive patients suggests that mild changes in olfactory identification may occur early in the course of HIV infection. In patients with clinical evidence of immunocompromise but without CNS HIV infection, olfactory identification deficits were also mild. Patients with HIV dementia, however, demonstrated a moderately severe deficit in olfactory performance that was not so severe as that reported in patients with Alzheimer's disease (9). These results are consistent with reports of early CNS involvement in HIV infection and suggest the potential for worsening olfactory performance with progression of HIV disease.

The etiology of diminished olfaction can reflect pathology from the nasal mucosa to the temporal cortex. Talano et al. (10), for example, recently reported changes in olfactory neurons that histopathologically resemble cortical abnormalities in patients with Alzheimer's disease. These data suggest not only that changes in the olfactory nerve may mediate decreased smell but that such changes may be reflective of alterations in higher cortical neurons. A primary role for hippocampal structures in olfactory memory was proposed by Baudry and Lynch (11). The case reported by Eichenbaum et al. (12) suggested a critical role for the temporal lobe in odor identification: after bilateral resection of the medial temporal lobe, their patient demonstrated profound difficulty naming common odorants but retained the ability to detect presence and intensity of odor. These findings point to potential areas of CNS pathology in HIV-infected patients.

Clinically, impaired olfaction might serve as a marker of early CNS HIV involvement. Future studies should attempt to match comparison and experimental populations for socioeconomic status and HIV risk behavior. In our small study group, although no attempt was made to ascertain HIV status in the comparison subjects, there is no reason to suppose that their rate of seropositivity would exceed that of the general population. Attempts to replicate the results reported here should also try to ascertain whether interventions aimed at reducing CNS morbidity improve olfaction. Such work would be important not only for the timing of appropriate interventions (e.g., zidovudine) but also for helping to elucidate meanings of olfactory disturbances in other disorders.

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Familial Association Between Attention Deficit Disorder and Anxiety Disorders

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Background and Method: This study tested hypotheses about patterns of familial association between attention deficit disorder (ADD) and anxiety disorders among 356 first-degree relatives of 73 clinically referred children with ADD and 26 normal comparison children. Through structured diagnostic interviews with trained raters, relatives were assessed for adult and childhood psychopathology. After stratifying the sample of ADD probands into those with anxiety disorders and those without, the authors examined patterns of aggregation of ADD and anxiety disorders in the relatives of these probands as well as in the relatives of the normal comparison subjects. Results: Familial risk analyses revealed that 1) familial risk for anxiety disorders was higher among all ADD probands than among the normal subjects; 2) familial risk for ADD was similar in the relatives of the ADD probands and of the probands with ADD and anxiety disorder; 3) the relatives of the ADD probands with and without anxiety disorders were at greater risk for ADD than the relatives of the normal subjects; 4) the risk for anxiety disorders was two times higher in the relatives of the probands who had ADD with anxiety disorder than in those of the ADD probands without anxiety disorders; and 5) there was a tendency for ADD probands' relatives who themselves had ADD to have a higher risk for anxiety disorders than ADD probands' relatives who did not have ADD (cosegregation). Conclusions: The results were most consistent with the hypotheses indicating that ADD and anxiety disorders segregate independently in families.
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Attention deficit disorder (ADD) is a heterogeneous chronic condition of unknown etiology associated with significant psychosocial and cognitive impairments; it is estimated to affect 6%–9% of school-age children (1, 2). A comorbid association between ADD and anxiety disorders has been found in epidemiologic (1) and clinical (3) samples of children with anxiety disorders and in samples of children and adolescents with ADD (4). Investigators have also noted higher rates of ADD among high-risk children of parents with anxiety disorders than in children of comparison groups (5). We recently reported a greater risk for anxiety disorders in ADD probands and their relatives than in normal comparison subjects and their relatives (4).

Converging evidence implicates a genetic component in anxiety disorders (6–8) and in ADD (4, 9–12). In a study of children with anxiety disorders, Last et al. (13) reported that mothers of anxious children had a significantly higher risk for adult and childhood anxiety disorders than mothers of normal children.

Family-genetic studies can provide external validation for a putative subtype of ADD based on the presence of a comorbid anxiety disorder and can help elucidate the nature of the association between the two disorders by testing competing hypotheses. In this study we evaluated the familial association between ADD and anxiety disorders and examined the following competing hypotheses: 1) ADD and anxiety disorders are etiologically independent (transmitted independently in families); 2) ADD and ADD with anxiety disorder share familial etiological factors, and ADD with anxiety disorder is a more severe disorder and therefore requires more familial etiological factors than the less severe ADD alone; 3) ADD and ADD

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TABLE 1. Predictions of Relatives' Risk for Attention Deficit Disorder (ADD) and Anxiety Disorders According to Six Hypotheses and Their Risk According to Study Findings

Condition	Relatives' Risk			
	ADD	Anxiety Disorders	Cosegregation of Disorders[a]	Nonrandom Mating
Hypotheses				
1. ADD and anxiety disorders are etiologically independent.			No	No
Probands with ADD	Increased	Not increased		
Probands with ADD and anxiety disorder	Increased	Increased		
2. ADD and ADD with anxiety disorder share familial etiological factors, but more are needed to manifest ADD with anxiety disorder.			Yes	No
Probands with ADD	Increased	Increased		
Probands with ADD and anxiety disorder	Very high	Very high		
3. ADD and ADD with anxiety disorder share familial etiological factors. The distinction between the two is attributed to noxious environmental factors that are not familial.			No	No
Probands with ADD	Increased	Increased		
Probands with ADD and anxiety disorder	Increased	Increased		
4. ADD with anxiety disorder is etiologically distinct from ADD.			Yes	No
Probands with ADD	Increased	Not increased		
Probands with ADD and anxiety disorder	Increased	Increased		
5. Probands with ADD and anxiety disorder are anxiety disorder patients who are misdiagnosed as also having ADD.			No	No
Probands with ADD	Increased	Not increased		
Probands with ADD and anxiety disorder	Not increased	Increased		
6. ADD and anxiety disorders are etiologically independent but co-occur at higher than expected rates because of nonrandom mating.			No	Yes
Probands with ADD	Increased	Not increased		
Probands with ADD and anxiety disorder	Increased	Increased		
Study findings			Yes	No
Probands with ADD	Increased	Increased		
Probands with ADD and anxiety disorder	Increased	Very high		

[a] "Cosegregation" indicates that disorders are transmitted together within families.

with anxiety disorder share familial etiological factors, and the distinction between the two is attributed to nonfamilial factors (i.e., noxious environmental factors that are not shared); 4) ADD with anxiety disorder is etiologically distinct from ADD without anxiety disorder; 5) probands who have ADD with anxiety disorder are patients with anxiety disorders who have been misdiagnosed as also having ADD; and 6) ADD and anxiety disorders are etiologically independent but co-occur at higher than expected rates because of nonrandom mating.

METHOD

The study method has been described in detail elsewhere (4). Briefly, the subjects were 73 Caucasian, non-Hispanic, nonadopted 6- to 17-year-old male outpatients consecutively ascertained from the pool of existing and new referrals at the Pediatric Psychopharmacology and Medical Pediatric Clinics of the Massachusetts General Hospital. These ADD probands met the *DSM-III* clinical criteria for the diagnosis of attention deficit disorder with hyperactivity (N=66, 90%) or without hyperactivity (N=7, 10%), with symptoms manifested at home and in school. Clinical diagnosis was based on interviews with the child and family by child psychiatrists (including J.B. and R.S.). The 26 normal comparison children were selected from pediatric primary care service referrals at the Massachusetts General Hospital and were screened for the absence of medical and psychiatric disorders. Individuals with mental retardation or chronic medical illness were excluded.

The probands and all available first-degree biological relatives of the ADD group (N=264) and the normal comparison group (N=92) were evaluated by raters who were blind to the clinical status of the probands. These psychiatric assessments of probands and their siblings were based on structured diagnostic interviews with the mothers in which the raters used the Diagnostic Interview for Children and Adolescents—Parent Version (14, 15). Diagnostic assessments of parents were based on direct interviews with each parent in which the raters used the National Institute of Mental Health Diagnostic Interview Schedule (16, 17) to evaluate adult disorders and an addendum based on the Diagnostic Interview for Children and Adolescents—Parent Version to evaluate childhood disorders. Diagnostic information was obtained for all siblings. Direct interviews were obtained from 99% (N=98) of the mothers and 75% (N=74) of the fathers. When one parent was not available, his or her diagnostic information was gathered from the available parent. Rates of illness reported here are lifetime prevalences. Parents were assessed for anxiety disorders both in childhood (separation anxiety, overanxious, and avoidant disorders) and adulthood (panic disorder, agoraphobia, obsessive-compulsive disorder, and phobic disorders). Interviews were conducted by four trained raters with undergraduate degrees in psychology. Interviews were audiotaped for random review and reliability assessments. Kappa coefficients of agreement between raters were greater than 0.95 for the diagnoses of children and adults, with the exception of major depression in adults (kappa=0.83).

Age-corrected rates of illness (morbidity risks) were calculated by using the Kaplan-Meier estimate from survival analysis (18). All analyses were two-tailed. Results were called statistically significant if the p value was less than 0.05. The six competing hypotheses could be tested on the basis of the familial patterns of aggregation of ADD and anxiety disorders found in the study (table 1). These hypotheses were derived, in part, from models of familial transmission presented by Pauls et al. (19) and Reich et al. (20).

RESULTS

Among the 73 ADD probands, 22 (30%) met the criteria for one or more comorbid anxiety disorders (avoidant disorder, N=3; obsessive-compulsive disorder, N=4; overanxious disorder, N=14; separation anxiety disorder, N=7; phobic disorder, N=12). We stratified the ADD probands into two groups: those with anxiety disorders (who had 74 relatives) and those without anxiety disorders (who had 190 relatives).

The ADD probands, the probands with ADD and anxiety disorder, and the comparison probands did not significantly differ in mean number of brothers (0.9, 0.6, and 0.7, respectively) and sisters (0.8, 0.7, and 0.8), and mean age of the probands (11.1, 9.6, and 10.5 years), of their parents (39.1, 37.0, and 37.9 years), or of their siblings (12.7, 12.4, and 10.6 years). The high rate of separation and divorce observed among the parents of the probands with ADD and anxiety disorder (59%) was significantly greater than the rates for the ADD (27%) and normal comparison (12%) probands. The proportion of direct interviews obtained from mothers was 98% for the ADD group and 100% for the other two groups. For fathers, the interview rates were 80% for the ADD group, 73% for the group that had ADD with anxiety disorder, and 65% for the normal comparison group. These proportions did not differ significantly among the three groups. There were no meaningful differences between the ADD probands with and without anxiety disorder in rates of comorbid conduct disorder (36% and 31%, respectively), major depression (32% and 24%), or dysfunction in school (68% and 80%).

Age-corrected morbidity risks for ADD did not differ significantly between relatives of the ADD probands and of the probands with ADD and anxiety disorder, but both were significantly higher than the risk for ADD in relatives of the normal comparison subjects (table 2). The risk for one or more anxiety disorders (child or adult) was significantly greater among relatives of the probands with ADD and anxiety disorder than among the relatives of the ADD probands. Both of these risks were significantly greater than the risk to relatives of the normal probands. The families of the children with ADD and anxiety disorder had the highest risk for one or more adult anxiety disorders, which was not statistically different from the risk to ADD children's families, but both were significantly greater than the risk to normal comparison families. A similar pattern was observed for the diagnosis of one or more childhood anxiety disorders. The risk to relatives of probands with ADD and anxiety disorder was significantly greater than the risk to relatives of ADD probands. Although relatives of both ADD subgroups had a higher risk for one or more childhood anxiety disorders than did the normal comparison subjects, only the comparison with the relatives of the ADD probands who had anxiety disorders attained statistical significance.

The risk for most individual anxiety disorders was higher in the families of the probands with ADD and anxiety disorder than in those of the ADD probands, but these differences failed to attain statistical significance (table 2). However, while the relatives of the children with ADD and anxiety disorder had significantly higher risks for overanxious disorder, panic disorder, and phobic disorder than the relatives of the normal comparison children, no significant differences for these disorders were found in comparisons between the ADD children and the normal comparison children (table 2). Among the relatives of all the ADD probands, the risk for one or more anxiety disorders was higher for mothers (31%) than for fathers (18%) and for sisters (8%) than for brothers (2%).

Among the relatives of all the ADD probands, the presence of ADD in a relative increased the risk for an anxiety disorder in the same relative (from 11% to 33%; z=3.4, p=0.0008). Thus, ADD and anxiety disorders were cosegregated (were not independently transmitted) among the relatives of the ADD probands. Evidence for cosegregation was observed for childhood anxiety disorders (presence of ADD increased the risk from 6% to 18%; z=2.5, p=0.01) and for adult anxiety disorders (increased from 13% to 20%; z=0.9, p=0.34), but the latter difference was not significant.

Among all families in this study, the risk for anxiety disorders among relatives was not significantly different for the various social class strata (21%, 12%, and 14% for high, middle, and low socioeconomic status, respectively; each p>0.10). Comparisons for specific

TABLE 2. Morbid Risk for Attention Deficit Disorder (ADD) and Anxiety Disorders in Relatives of Study Probands

	Morbid Risk (%)					
	Relatives of Probands With ADD and Anxiety Disorder (N=74)		Relatives of ADD Probands (N=190)		Relatives of Normal Comparison Subjects (N=92)	
Disorder	Risk	SE	Risk	SE	Risk	SE
ADD[a]	23.0	5.2	25.9	3.3	4.6	2.3
Anxiety disorders						
Any disorder[b]	29.0	6.3	14.7	3.1	5.3	2.6
Any adult disorder[c]	27.5	7.1	13.1	3.6	3.9	2.7
Any childhood disorder[d]	16.7	4.8	6.4	2.0	2.6	1.8
Agoraphobia (parents)	3.9	2.8	5.0	2.0	1.5	1.5
Panic disorder (parents)[e]	12.9	5.0	4.6	2.4	0.0	0.0
Phobic disorder[f]	13.0	4.8	5.5	1.9	1.1	1.1
Avoidant disorder	1.5	1.5	1.2	0.9	0.0	0.0
Obsessive-compulsive disorder	2.4	2.4	0.0	0.0	0.0	0.0
Overanxious disorder[g]	13.9	4.6	5.2	1.8	1.4	1.4
Separation anxiety	7.8	3.3	1.7	1.0	1.1	1.1

[a] Significant difference between relatives of probands with ADD and anxiety disorder and those of comparison subjects ($z=3.2$, $p=0.001$) and between relatives of ADD probands and those of comparison subjects ($z=5.3$, $p=0.000$).

[b] Significant difference between relatives of probands with ADD and anxiety disorder and those of ADD probands ($z=2.0$, $p=0.04$); between relatives of probands with ADD and anxiety disorder and those of comparison subjects ($z=3.5$, $p=0.0005$); and between relatives of ADD probands and those of comparison subjects ($z=2.3$, $p=0.02$).

[c] Significant difference between relatives of probands with ADD and anxiety disorder and those of comparison subjects ($z=3.1$, $p=0.002$) and between relatives of ADD probands and those of comparison subjects ($z=2.0$, $p=0.04$).

[d] Significant difference between relatives of probands with ADD and anxiety disorder and those of ADD probands ($z=2.0$, $p=0.05$) and between relatives of probands with ADD and anxiety disorder and those of comparison subjects ($z=2.7$, $p=0.006$).

[e] Significant difference between relatives of probands with ADD and anxiety disorder and those of comparison subjects ($z=2.6$, $p=0.01$).

[f] Significant difference between relatives of probands with ADD and anxiety disorder and those of comparison subjects ($z=2.4$, $p=0.02$).

[g] Significant difference between relatives of probands with ADD and anxiety disorder and those of comparison subjects ($z=2.6$, $p=0.01$).

anxiety disorders also failed to reveal significant differences in socioeconomic status. Regarding family intactness, the risk for an anxiety disorder was similar among the relatives in nonintact and intact families (13% and 16%; $z=0.5$, $p=0.60$), and the same was true for adult and childhood anxiety disorders separately. Fathers with ADD were not more likely to have spouses with anxiety disorders than fathers without ADD (28% and 39%, respectively; $p=0.44$, Fisher's exact test). Similarly, the presence of ADD in mothers did not predict anxiety disorders in fathers ($p=1.00$, Fisher's exact test).

DISCUSSION

Our data indicate that 1) the overall risk for anxiety disorders among the relatives of patients with ADD was significantly higher than the risk among relatives of the normal comparison subjects; 2) the risk for anxiety disorders was greater among the relatives of ADD probands with anxiety disorder than of those without; 3) families of both ADD probands and probands with ADD and anxiety disorder had significantly higher risks for anxiety disorders than did the relatives of the normal children; 4) there was a tendency for ADD and anxiety disorders to cosegregate within families; and 5) there was no evidence for nonrandom mating.

The present findings are partially consistent with hypotheses 2 and 4 (table 1). Hypothesis 2 correctly predicts that there will be higher rates of anxiety disorders among families of probands with ADD and anxiety disorder than among families of ADD probands and that both will have rates greater than relatives of normal comparison subjects. Cosegregation is also correctly predicted by this hypothesis. However, it incorrectly predicts higher rates of ADD among the relatives of children with ADD and anxiety disorder than among the relatives of children with ADD alone. That is, if ADD with anxiety disorder is a more severe form of ADD, we would have expected the relatives of children with this diagnosis to be at greater risk for both ADD and anxiety disorders than the relatives of ADD probands; however, this was not the case in this study. Our results are also partially consistent with hypothesis 4, which correctly predicts high rates of ADD among relatives of both subtypes, higher rates of anxiety disorders among relatives of probands who have ADD with anxiety disorder, and cosegregation of ADD and anxiety disorders within families. However, it cannot easily explain the higher risk for anxiety disorders among the relatives of the ADD probands than among the relatives of the normal subjects.

Although our data cannot fully discriminate between hypotheses 2 and 4, the other hypotheses are much less consistent with the observed results. The significantly higher risk for anxiety disorders among relatives of ADD probands than among relatives of normal subjects is not consistent with the idea that ADD and anxiety disorders are etiologically independent (hypothesis 1). Since a higher risk for anxiety disorders was observed among relatives of children with ADD and anxiety disorder than among relatives of ADD children, it seems unlikely that the two disorders share common etiological vulnerabilities (hypothesis 3). The ADD in our probands with ADD and anxiety disorder is not likely to have been secondary to the anxiety disorder (hypothesis 5), because one would not expect secondary ADD to exhibit familial transmission as was observed in this study. The lack of evidence among the parents for nonrandom mating with regard to ADD and anxiety disorders argues against the hypothesis that ADD and anxiety disorders are etiologically independent but co-occur at higher than expected rates due to nonrandom mating (hypothesis 6).

Although in the context of hypothesis 3 the familial analyses do not implicate environmental influences in the etiology of ADD with anxiety disorder, we cannot rule out the influence of environmental factors (21). We previously reported that the greater risk for ADD among relatives of ADD probands could not be accounted for by social class or intactness of the family of origin (4). In this study we found that neither social class nor intactness of the family could account for familial transmission of anxiety disorders. However, since the scope of psychosocial dimensions we assessed was limited, more work is needed to further clarify the role of psychosocial adversity in the familial association of ADD and anxiety disorders.

Our findings are consistent with a number of observations in the literature. Although family studies of adult probands do not usually evaluate the presence of ADD, the co-occurrence of ADD and anxiety disorders has been reported by other investigators in studies of high-risk children of parents with anxiety disorders (5, 22). The co-occurrence of ADD and anxiety disorders was also found among children clinically referred for anxiety disorders (3) and in an epidemiological sample of nonreferred children from the general population (1).

Our findings, based on a clinical population, should be interpreted with caution, since they may not be generalizable to other populations. Clinically referred children with ADD are more likely to be severely ill and to seek treatment from a physician or other health professional than nonreferred ones. In particular, anxious parents may be more likely to refer ADD children for treatment than nonanxious parents. Although such a referral bias is possible, similar findings in nonreferred children (3) suggest that such a bias may not entirely account for our results. More work needs to be done on referred and nonreferred samples to further clarify this issue. Given that ADD is associated with several comorbid disorders (e.g., major depression, conduct disorder, oppositional disorder), the observed familial association of ADD and anxiety may be mediated by another comorbid disorder. To adequately address this multivariate issue, a much larger sample size than the one reported here will be required.

Although the validity of retrospective diagnoses of ADD and childhood anxiety disorders in adults has not been extensively documented, several studies have shown that it is possible to diagnose these disorders in adolescents and adults by using structured interview techniques (13, 23–25). Despite these limitations, our findings retain considerable validity. The assessment of psychopathology in probands and relatives was made according to criterion-based, structured interviews, and all diagnoses were made by raters who were blind to the clinical status of the probands. The instruments we used were similar to those used in large epidemiologic studies of adults and children, and the rates of disorders found in the normal comparison children and their relatives were compatible with the rates in those studies (1, 26).

Confirmation of these findings has potentially important implications for the field. Future studies on ADD children and anxious children may benefit from an evaluation of comorbid diagnoses. The identification of a subgroup of "high-risk" ADD children may permit the development of early intervention programs. For clinical practice, the identification of more homogeneous subgroups may permit a more rational approach to treatment. For example, there is evidence that stimulants are detrimental to anxious ADD children, most likely because stimulants are anxiogenic (27, 28). For such children, tricyclic antidepressants may be more helpful than stimulants (29).

In conclusion, in a group of clinically referred children and adolescents with ADD, familial risk analyses revealed that relatives of ADD probands with anxiety disorders had a similar risk for ADD but a greater risk for anxiety disorders than relatives of ADD probands without anxiety disorders. Both subgroups differed from relatives of normal comparison subjects in the rates of these disorders. Further work is needed to clarify the role of comorbid anxiety in the familial transmission of ADD and to evaluate the role of other biological and clinical factors that may mediate this comorbidity.

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Book Forum

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PSYCHOANALYSIS

Reading Freud: Explorations and Entertainments, *by Peter Gay. New Haven, Conn., Yale University Press, 1990, 198 pp., $24.95.*

This is a book of varied, uneven, and predominantly interesting essays around the margins of the author's major biography of Freud (1). In eight essays, a prefatory note, two introductions, and some scholarly apparatus, Gay discusses Freud's naming of his six children; Freud's late-life enthusiasm for the earl of Oxford as the author of Shakespeare's plays; the possibility that Freud had an affair with Minna, his wife's sister; and Freud's listing of 10 good books in answer to a questionnaire. Gay also studies Freud's relationship to freedom and free will; takes a brief look at Freud and jokes; provides an unserious, brief elaboration of Freud's remark that had he had the Gentile name of Oberhuber, his works would have met far less resistance; and reprints his spurious 1900 review of *The Interpretation of Dreams.*

The last of these created some controversy among a few scholars and others after it was published in *Harper's* magazine in 1981 (2), in a format that was considered humorous by some and fraudulent by others. It was presented in *Harper's* as a newly discovered unsigned review from an obscure Austrian medical journal, a made-up journal with a name suitably banal to Austrian ears and rather splendid to American ears: the *Grazer medizinische Vierteljahresschrift* 1900; XVIII(3 [July]):139–148. Some subsequent scholars, unable to find that journal, have been annoyed at Mr. Gay. Their ancestors were probably similarly miffed at not being able to find Dr. Ralph, who, Voltaire tells us, wrote *Candide.*

Mr. Gay points out in the present volume that had he really struck such a piece of scholarly gold, he would have "called a press conference and published the piece in a learned journal" (p. 130). This is very likely true, but part of the provocative quality of the spoof is in the fact that some scholars just might publish a powerful scholarly discovery in a place like *Harper's.*

The content of the review of *The Interpretation of Dreams* seems to me too learned, balanced, even prophetic, to be believable as the product of an earnest, probably provincial Austrian doctor publishing in a second- or third-rank journal in 1900. The temptation for Gay to write a thoughtful review (quite valid, I think) seems a far stronger force than the temptation consistently to stay within the bounds of what someone like an internist in Graz in 1900 might have known and thought. Adding another twist, in a subsequent, not quite serious essay, Gay refers to this review again and implies that Freud himself anonymously wrote it (a nice idea, probably again aimed partly at tweaking scholarly noses). At any rate, Gay's review is, if not quite 1900 and not quite 1981, mostly a good and well-informed review of *The Interpretation of Dreams.* It must have been fun for a Freud scholar to write, with or without its spoof framework and escape hatches.

The essays on Freud's choosing names for his six children and on Freud's "10 good books" seem to me good ideas not fully lived up to. Gay discusses naming, Jewish naming, and some of Freud's style and roles, such as being himself firmly in charge of naming his children. There is consideration of Freud's perhaps naming his own final sibling, Alexander, and of his naming his sons Jean Martin (after Charcot), Oliver (after Cromwell), and Ernst (after Brücke). But three of Freud's children were female; Gay is remarkably less interested in these three names as names or for whom they were named. He discusses them far less than the male names and cites their namesakes as faceless appendages to the men in their lives: Mathilde was named after "Breuer's wife," Sophie after "a niece of Samuel Hammerschlag," and Anna after "one of Hammerschlag's daughters." Even if this may partly echo Freud's patriarchal style, it slights the daughters and our interest in them.

As to Freud's list of 10 books, the idea of knowing about Freud through his reading is a major and challenging one, probably unworkably vast, but the list of 10, with Gay's discussion of it, is only something of a *jeu d'esprit* at the edge of that larger subject. Typical of Freud was his response to being asked for a list of 10 good books: he analyzed the request and decided it meant not 10 "most magnificent" works of world literature (such as *Hamlet,* Freud suggested), not 10 "most significant" books (such as Darwin's *Descent of Man*), and not even 10 "favorite" books (such as *Paradise Lost* or Heine's *Lazarus*). He decided that the request was for good books somewhat analogous to good friends, "to whom one owes a portion of one's knowledge of life and one's world view" (p. 98). Gay reasonably points out that the unpretentiousness of Freud's choices is something of a guarantee of their authenticity. I will not list the 10 here (educated readers of modern English or American works will probably have read two of the 10), but Gay makes historically and analytically useful comments and speculations about them and their authors in Freud's intellectual life.

"Freud and the Man From Stratford" is the longest essay in the book, and even for those of us who think Freud's endorsing of the earl of Oxford was very likely wrong, and a bit of a hobbyhorse, Gay provides thoughtful notes on Freud and Shakespeare, on authors and their works, and on the particular book and arguments that seemed most persuasive to Freud.

"Freud and Freedom," a challenging topic, is an essay seemingly more philosophical and less historical than most of the others, but actually especially useful, I think, for Gay's usual fluent amassing of pertinent Freudian comments over time. As a philosophical or psychoanalytical question, the topic needs far more than the 20 pages allotted to it and has received longer discussion elsewhere.

The essay on Freud and jokes, "Serious Jests," also a bit short for its aims, retells a few good Freudian jokes, condescends oddly about a few, and recapitulates a bit of Freud's book on jokes. It publicizes one nice little mystery that I hope someone may soon solve: What is the meaning of the punch line and what is the joke regarding which Freud wrote Fliess the following punch line in his letter of Sept. 21, 1897: "Rebecca, take off your dress, you aren't a Kalle—bride—any more" (p. 133)?

Finally, we come to the essay on Freud's possible affair with his sister-in-law. This essay adds little to what many people hope is a juicy little morsel of gossip. Gay discussed his thoughts in his biography of Freud (affair unlikely, and not very important one way or the other to Freud's theories) (1). His subsequent reading of a good many previously unavailable letters between Freud and Minna has not changed his view. A mystery remains in this area, though, larger and different from the little one. Gay notes that years of the Freud-Minna letters are missing, although someone seems once neatly to have numbered them all sequentially. What was in those letters? Did Anna Freud or someone else destroy them? It seems to me that the gaps are not likely to have been accidental, which certainly adds to one's eagerness to know what—about an affair, perhaps, but certainly about other matters—was in those letters. Gay seems less interested than I would have expected him to be in solving that gap. Perhaps, as an energetic scholar at the end, he says, of his Freud biographical period, he is resigned to the fact that some things are lost and may always remain beyond our knowledge.

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Freud: A Life for Our Time, *by Peter Gay. New York, W.W. Norton & Co, 1988, 786 pp., $35.00; $14.95 (paper).*

There has been a great surge of intellectual interest in psychoanalysis in recent years as scholars try to understand its meaning and significance for the disciplines of the humanities and the sources of its continuing cultural influence in the Western world. As a result of this effort, Freud scholarship has burgeoned during the past decade, aided by the availability of new material, such as the complete letters to Fliess, the biographies of Klein, Anna Freud, and Bonaparte, and the memoirs by Kardiner, Wortis, and Sterba. There have been important studies on the origins of Freud's thought and the nature of his literary exposition, and there has been renewed scrutiny of Freud's cases. We now know a great deal about who some of his patients were, their backgrounds and what became of them, as well as how Freud thought about them before shaping the material for publication (e.g., the Rat Man) and of Freud's personal influence in some of his patient's lives (e.g., the Deutsch-Tausk episode and the case of Frink). The passage of time has helped to curb some of our less modulated idealizing or denigrating tendencies so that we may begin to develop a picture of Freud in his full humanity, including a generous array of human foibles, without destroying his heroic stature. We have been through such controversies as whether Freud did or did not sleep with his sister-in-law (probably not), whether he did or did not lie about his patients' childhood seductions (almost certainly not), whether he did or did not fudge some aspects of his case presentations to suit his theoretical needs (almost certainly he did), and his extraordinary idea of analyzing his daughter (and worrying about why she did not marry). When the dust of these gusts has settled we remain with an undamaged sense of this intellectual giant and his achievement.

Against this background, Peter Gay has written a magisterial biography of Freud that has at least three major strands: a depiction of Freud's life, a description of the growth of psychoanalytic ideas, and a delineation of the mutual influences of the man, the ideas, and the times. Although the book is presented to us as a life, I suggest that is the lesser of its great achievements. Even more stunning are the descriptions of the growth of psychoanalytic theory, including concise and precise glosses and abstracts of Freud's papers, monographs, and developing ideas and the beautiful interweaving of the ideas with descriptions of Freud's life and with the history of the period. No one else has provided such a vivid sense of psychoanalytic ideas as living and conflicting entities, born and growing largely within Freud's mind; the person and the ideas are coextensive. In many ways this book is the best précis of psychoanalysis available; all of the major works are summarized and abstracted.

Gay is, of course, a master at elucidating the cultural and political landscape within which psychoanalysis grew to such dominating height, and we come away with a full, lively, and intricate sense and understanding of Freud within his epoch. Gay presents a picture of Freud more complex and more useful than any before, a "warts and all" vision of Freud the man, who, alongside his nobility and generosity of spirit and mind, could be mean, vengeful, and narrow. Gay's confidence in the greatness of the man and his discoveries helps him to relinquish any desire to color the material or to blur Freud's flaws. The Freud who comes through to us is a man of lifelong defiance, with a breadth of interest that is still astonishing. We also get a picture of a bit of the private man, worrying about his children, suffering hugely over the deaths of a child and a grandchild, endlessly enjoying Anna. On the other hand, except for Anna, the women in Freud's life—his mother and wife—do not come to life the way others in the story do. We still miss any sense of who Mrs. Freud was and what kind of a life she led, overshadowed by her daughter and perhaps her sister-in-law. Presumably the information is simply not available.

Although the book is subtitled *A Life for Our Time,* it might more accurately be labeled *A Work for Our Time.* The author's introduction to chapter 10 illustrates his methods: "The questions that preoccupied Freud from the mid-1920s on were not pure abstractions for him, but acquired their urgency from events in his personal life. They exhibit once again the continuous traffic in Freud's mind between private feelings and scientific generalizations—the traffic that reduced neither the intensity of his feelings nor their relevance to his science. Beneath the surface of his rational argumentation, there lurks Freud the disappointed father, the concerned mentor, the anxious son" (p. 470). It is this interweaving that Gay superbly lays before us. On the other hand, we know little from this book about Freud's formative years that we did not know before. Gay gives relatively scant attention to Freud's early scientific career, or to his even earlier philosophical enthusiasms. Gay gives us excellent vignettes of bits and pieces of young Freud, but one has the impression that he is uninterested in the life of the child, boy, and young man before that life was involved with psychoanalysis. By page 50 of this work of almost 800 pages, we are already at the period of Freud's involvement with Charcot. Of course, it is far more difficult to know much of early Freud, but this structure to the biography emphasizes that the author is interested in psychoanalysis and the intellectual life of the man who created it, and he generally avoids the psychoanalytic speculations of a "psychobiographical" essay that might attempt to understand the origins of the genius—a challenge that Freud could not resist.

I believe it is a merit of this book that it is written primarily as history and not psychodynamics; that would be a different biography. Once psychoanalysis is a part of the story, Gay is much more enthusiastic in his portrayal of the man who is inseparable from his discoveries. However, Gay is perhaps excessively devoted to Freud's own accounts of himself in his writings. At times in the biography one longs for a better sense of how others saw him. Of course, no one could write more vividly than Freud did about himself.

Gay brilliantly describes Freud's revolutionary psychology, clarifying that Freud, far from being antiphilosophical, had major philosophical goals. His dispute with philosophy was with speculative metapsychology, and his revolution was to describe a deterministic scientific psychology built on psychological premises, neither metaphysical nor physiological. Although Gay may underplay the importance of "The Project" and its neurological underpinnings as a conceptual framework that Freud never fully abandoned, he is right to stress Freud's emphatic and revolutionary view of the mind as an object for scientific study. In 1896 Freud wrote to Fliess, "I see how you, through the detour of being a physician, are reaching your first ideal, to understand humans as a physiologist, just as I most secretly nourish the hope of reaching my original goal, philosophy" (p. 118). Freud never abandoned philosophy; rather, he redefined it. He intended nothing less than to unriddle the mind, a task he loved for its intellectual beauty and for its potential human good. Freud was serious about his desire to relieve human suffering. Gay demonstrates that Freud, early in his sexual investigations, saw himself as a "physician to society" (p. 63), leading the way to a healthy and liberating sexuality.

Gay portrays a man who simultaneously valued his findings and theories as among the great human discoveries, was impatient with those who could not or would not give him adequate credit, and endlessly wrestled to repair the inconsistencies and shortcomings of his theories revealed by his own continuing gathering of analytic data. That extraordinary tolerance of ambiguity, so rare in much of the psychoanalytic movement, was crucial for Freud's capacity to retain the leadership of his field. The hegemony that Freud retained over psychoanalysis throughout his lifetime was not simply the result of his charismatic and ambitious character; it was even more a consequence of his capacity to entertain new ideas even when they had the effect of putting his old ideas in question. As the inventor and discoverer of psychoanalysis, Freud was always willing—in fact, inwardly compelled—to replace old ideas with new ones (preferably of his own creation), unable to blink away intellectual problems for very long. His followers, on the other hand, were usually in the position of finding themselves with abandoned belief systems as they failed to keep up with the master.

This biography gives a fresh sense of Freud and psychoanalysis within its own time. It is startling to read quotes from the *New York Times* in the 1920s indicating that Freud was already something of a pop culture hero, an accepted part of the intellectual avant-garde, and that events in the world of psychoanalysis were the stuff of headlines and photographs, a part of the daily news in American life. This is not the picture that Freud enjoyed of himself as embattled and never quite victorious. That Freud tended to denigrate his American popularity does not diminish the fact of it, and it may help to temper the spirit of martyrdom that occasionally colors the view of psychoanalysts who like to think of themselves as continuing in Freud's isolation. Freud required a myth of isolation to retain the self-representation as radical iconoclast that fired his independence of thought. Social acceptance threatened his creativity. Freud's stature as discoverer-founder of a field of science, leader of an intellectual movement, a preeminent culture hero who embodied the conflicts and the visions of his times, as well as the first psychoanalyst, has been in some ways a misleading model for psychoanalysts. Although not many analysts think of themselves as Freud, we all more or less think of ourselves as Freudian, and many in our profession have tried to live our lives in a "Freudian style," forgetting that the way Freud lived his analytic life was a consequence of being Freud and is not available to the rest of us. One of Gay's great achievements in this biography is the rich, almost cinematic sense of the older Freud in all his poignancy as he struggles with his changing ideas and his cancer and impending death, refusing all self-pity and, where necessary, engaging in extraordinary denial of the world around him to protect his energies for his work and his closest family and friends.

This Freud biography seems to me to have a universal appeal. Students new to psychoanalysis will learn a great deal about both Freud and psychoanalysis. Experienced clinicians and psychoanalysts will find stimulating reminders of the structure, complexity, and incompleteness of Freud's thought and the extraordinary insights that fueled his theories. Students of intellectual history will enjoy this account of one of the great intellectual journeys beautifully set within its intellectual landscape. Readers who like adventure stories will find few that are more exciting. In other words, everyone will enjoy and learn from Peter Gay's extraordinary biography of Freud.

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Psychoanalytic Explorations: D.W. Winnicott, *edited by Clare Winnicott, Ray Sheperd, and Madeleine Davis. Cambridge, Mass., Harvard University Press, 1989, 602 pp., $39.50.*

I met D.W. Winnicott one time, and it was an experience I shall never forget; it lends to everything he wrote a special context for me. He had just given a paper at a conference, and afterward I went up to him to describe an idea of my own related to what he had been saying. He suggested we walk back together to his hotel so that we could continue our discussion. During all of our ensuing conversation he held me in the center of his attention (or so it seemed to me) in a way that I have never experienced with any other human being. It was not that he made constant eye contact, or that he interjected the traditional psychoanalytic hum of empathy, or that he was selflessly accepting. As we walked he spoke of his own ideas, he reacted and responded with dignity and originality, yet all the time I felt recognized and encouraged—I was in a "facilitating environment." Quite unexpectedly he said to me, "Dr. Stone, we will have to stop for a moment. I have terrible angina." His face was white with the pain, but then with amazing equanimity he continued as before.

Winnicott is best known for his description and formulation of the transitional object and transitional phenomena. His basic text was the mother-infant relationship, and he learned and taught from it as much as any modern thinker. He apparently recognized that the central problem after Freud was the concept of object relations—the mystery of the other. Although he wrote on many subjects, his most important legacy is, I believe, to our understanding of the development of object relations.

The present volume contains unpublished papers and drafts that are printed here 18 years after his death. Winnicott's major failing as a scholar was that he went his own way, making no systematic effort to relate his own work to that of others. Four years before his death, in a talk to his senior colleagues transcribed in this volume, he spoke of trying to "make amends and join up with the various people all over the world who are doing work which either I have stolen or else I'm just ignoring." He was never to make good on this attempt, however; like many other original thinkers, including Freud, he marched to his own drummer.

Winnicott's published papers were often brief. He opened a door to a subtle but important phenomenon, deployed language in a unique way, and had a philosophical bent concealed under a clinician's simple feel for his subject. The same qualities will be found in the present collection, although many of the papers are even more cryptic and telegraphic than his published work. The editors have included some published reviews that give at least a sense of his reactions to other major contributors. Also presented here are his writings, filled with moral fervor, against the initial British enthusiasm for lobotomy and ECT. Perhaps most interesting to his readers will be the series on the use of the object. These papers demonstrate the admixture of psychoanalyst and phenomenologist that made his best work truly memorable. The true value of this volume, however, will be found by those who care enough about Winnicott to want to get a sense of how his mind worked. They will discover, I think, that his greatest failing was his greatest strength. Inspired by some connection between a clinical problem, a footnote in Freud, a poem of Rilke, how a patient made him feel, and an analysis of one of his own dreams, he would produce an original idea. Many of these ideas are obscure, but some go to the heart of the matter even if they ignore other writers who got to the same place by a different route.

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The Annual of Psychoanalysis, vol. XVII, 1989, *edited by the Chicago Institute for Psychoanalysis. Hillsdale, N.J., Analytic Press, 1989, 342 pp., $36.00.*

The 17th volume of *The Annual of Psychoanalysis*, issued by the Chicago Institute for Psychoanalysis, begins with a section on Theoretical Studies. In the first chapter, John Gedo mounts a radical critique of psychoanalytic theories of transference, whether based on the traditional transference neurosis or on Kohutian archaic transference. Different as these are in other respects, both depend on the concept of the neutral, noninvolved analyst, and for Dr. Gedo "analytic 'neutrality' is not merely an unattainable theoretical fiction: it is also a mischievous notion that leads us into an epistemic never-never land" (p. 8). The complex interactions between analyst and analysand have been mistaken for "static internal conditions characteristic of the analysand" (p. 13), and it is time to end this fiction by proper attention to contributions from both members of the dyad. Although possibly underestimating the extent to which a reasonable degree of neutrality can be achieved by the analyst, Gedo expresses views here that are a salutary corrective of what has been a psychoanalytic sacred cow. It should be mentioned, however, that his paper confirms a remark of Leston Havens about Harry Stack Sullivan as the most influential but least acknowledged analyst in the United States, since what Gedo is espousing without referring to Sullivan is the essence of interpersonal theory.

This rousing initial contribution is followed by Edwin Wallace's attempt, using a phenomenological approach, to prune psychoanalytic theory to a lean and minimal level compatible with clinical and common-sense observations and treatment activity. Wallace eschews as unnecessary and even incorrect the more radical critiques of Schafer and Spence. Although obviously not a Kohutian, Wallace is cautiously respectful of Kohut's contributions. Dr. Wallace's essay is abstract, dense, and detailed; it is not easy reading but commands respect and will be of interest to psychoanalytic theorists. To my mind, the essay neglects an opportunity to integrate current notions about the biogenetic roots of many forms of psychopathology within psychoanalytic formulations. For instance, can a case really be made any more for considering schizophrenia an oral derivative?

The section on Applied Psychoanalysis is led off by Drs. Mavis and Harold Wylie's exploration of the dynamics underlying the marked contrast between the first and third naturalistic periods in the work of the Norwegian artist Edward Munch and his middle Expressionistic phase (in which he painted the well-known *The Scream*). The Wylies attribute these vicissitudes in Munch's creativity to unresolved conflicts over the death of his ambivalently regarded father and Munch's pattern of seeking and then rejecting father surrogates. This formulation is plausible; however, based as it is on a study of Munch's paintings and journals and not at all, obviously, on any direct observation of the artist, let alone a psychoanalytic interchange with him, the formulation is expressed with a certainty and unequivocality that have a grating quality. There is something solipsistic about this kind of approach to applied psychoanalysis. Is it not possible that a Munch on the couch might have produced some unanticipated surprises?

Jerome Winer uses the relationship between Romola and Savonarola in George Eliot's novel *Romola* as the basis for a psychoanalytic theory of charismatic fellowship. He views this fellowship as a three-stage process initiated by an acute personal crisis activating an unconscious fantasy of enforced passivity, followed by an unstable identification with a charismatic leader, and closing either with depression or an active taking on of the charismatic qualities of the leader.

Dr. Winer here is advancing a theory about a psychological phenomenon using the characters in a novel for illustrative purposes (although the line between illustration and evidence can become murky) rather than drawing conclusions about real persons without having examined them, as is done by the Wylies. This theory, therefore, could putatively be supported or denied by psychoanalytic study of such instances.

In "On Migration—Voluntary and Coerced," George Pollock attempts to apply to the forced emigration of exiles so characteristic of our troubled times his research of many years on what he has designated the mourning-liberation process. This is a normal adaptation to change and loss, which under certain conditions can become pathological. Forced emigrations are always marked by ambivalence because the emigrant both clings to and must give up what is left behind in trying to adapt to the new. Obviously there is more potential for pathological reactions when the migration is involuntary rather than voluntary, but there are common elements such as culture shock and mourning the lost motherland. The mourning-liberation process in these instances can be marked by a sense of nostalgia whose effects range from depression to an adaptive, even creative, end product. The area Dr. Pollock is treating is an important one to which he has given much thought: this paper, however, suffers to some extent from being based on an overly condensed summary of a considerable body of previous work.

The section on applied psychoanalysis is completed by Martin Nass's critique of psychoanalytic attempts to understand creativity in general and musical creativity in particular. He notes the difficulty in understanding creativity in the absence of direct evidence from the psychoanalysis of artists and emphasizes such methodological errors as an emphasis on conflict over talent and the reductionistic arrogance of analysts who feel that their methods can explain a field about which they themselves have little or no knowledge. Nass's review of the literature in psychoanalysis and music reveals its thinness and the lack of any sort of central consensus about the process of creativity in musical productions. Nass does not ignore the role of conflict as an influence in musical and creative expression, but he feels that the creative act is primarily an autonomous function.

The first paper in the most directly clinically oriented section of the book, Psychoanalysis and Parenthood, is a vigorous and well-documented attack on what F. Diane Barth sees as the psychoanalytic sin of parent blaming. This practice is a covert consequence of some aspects of object relations and interpersonal theories, particularly those of Kohut. Parent blaming in this sense is a reaction to the equally reductive practice of instinct blaming derived from Freud's drive theories. Barth makes it clear that both forms of blaming are inimical to the proper and appropriate psychoanalytic activity of helping the patient develop personal responsibility and understanding. From my own experience, Barth's point is well taken and leads to speculation about why analysts need something or someone to blame. Can the persistence of blaming despite basic theoretical differences be a consequence of the difficulty that psychoanalysts find in bringing about real and constructive changes in some patients? Blaming then serves the purpose of exculpating the treatment from its lack of success in these cases.

In the next paper, Helen Beiser takes as her subject matter the many accounts in both the Old Testament and the New Testament of the substitution of symbolic for direct sacrifice of the firstborn son, starting with the story of Abraham and Isaac. For Dr. Beiser these accounts suggest that a fundamental ambivalence rather than simple oedipal hostility and fear resides in the father-son relationship. She sees Biblical fathers as expressing an emotional preference for the younger son over the firstborn son that is at odds with the legal preference for the rights of the latter. This ambivalence of the firstborn son toward his own father, experienced as a need to propitiate the latter, complicates the transition from the role of firstborn son to that of father of the firstborn. Dr. Beiser's argument, while illustrated by the examples she provides (there may be a factor of selectivity at work here), shares the defect I have previously mentioned and is admitted by Dr. Beiser—it lacks any grounding in clinical psychoanalytic evidence.

The first contribution to the fourth section of the volume, Psychoanalysis and Gender, is an important paper by Nancy Chodorow with discussions by Barbara Rocah and Bertram Cohler. Dr. Chodorow takes as her starting point the differing views and failures of communication that exist among the various groups interested in femininity as a psychoanalytic concept. The failures of communication, Dr. Chodorow notes, occur particularly between psychoanalysts and feminists from other disciplines. One important focus in her paper is the disagreements between classical psychoanalysts on the one hand and object relations theorists (among whom she counts herself) and interpersonal theorists on the other. These latter two groups agree in emphasizing that femininity is derived from a gender rather than a purely sexual difference and that it develops along with other aspects of selfhood from early experience, principally within the infant-mother dyad. In the other camp is the psychoanalytic view, which even in its more sophisticated post-Freudian guise emphasizes the importance of anatomical sex differences and still holds that anatomy is destiny.

Dr. Chodorow concludes by urging that the opposing camps—those trained in psychoanalysis in a broad sense and those from other disciplines—take a less polemical view of each other's work so that their contributions can fructify rather than interfere with their mutual efforts to facilitate the emergence of the image of women in psychoanalysis from its early and incorrect Freudian origin.

Dr. Chodorow's paper is less parochial and of more general interest than many of the others in this volume. My review can do no more than pay tribute to its wide-ranging erudition and closely reasoned argument. My only reservation is the absence of any discussion about possible prenatal hormonal influences on personality differences between male and female children in, for example, aggressiveness.

Wendy Doniger, using as illustrative material the story of Rachel and Leah, both in the Biblical and Midrashic versions, along with a number of Hindu myths explores the meaning underlying the frequent accounts in these stories and others of doubling, surrogating, and masquerading by both men and women in sexual encounters. A constant in all these myths is the tension between the need and desire to remain whole and the opposite need to split as a way of resolving the ambivalence resulting from this tension. Relief through splitting, however, is short-lived because it becomes the source of new conflict leading, in a dialectic way, to reuniting. Dr. Doniger deploys her material skillfully and gracefully as she expands on the different purposes and strategies of men and women in these situations of conflict between sexual roles. There is an implication, remarked upon by Harry Trosman in his discussion, that women find more gratification in integration and men more from the satisfaction available to their singular halves resulting from the split.

The final section, Psychoanalysis and Child Development, consists entirely of a paper by E. Virginia Demos with discussions by Marian Tolpin, Marjorie Barnett and Bertram Cohler. Relying on the extensive research in child development led by Louis Sander, in which she has been involved, Dr. Demos describes the "infant of the eighties" (who also may be called the "Sander baby") as being quite different from the Freudian baby, who is essentially passive, without a self structure early on, motivated primarily by a need for tension reduction, and with what may be called a "pathomorphic" course of development. The "eighties" infant has a self structure from the beginning along with a much more sophisticated behavioral repertoire and actively seeks stimuli. Dr. Demos stresses the motivating force of affective states in development as the infant seeks to reduce negative affective states and to maximize positive ones. These efforts lead to complex interactions with caretakers in which certain sequences (after frustration of a pleasurable experience parents comfort or guide the child) encourage self-confidence and innovation but others (the frustration is ignored or punished by the parents) lead to timidity and excessive caution. This paper is wide-ranging and informative and could be read with profit by anyone, psychoanalyst or not, who is interested in child development and its adult consequences. It should be said, however, that the view of human development and potential that it advances is rather sunny and optimistic and may be ignoring the effects of relatively intractable internal tensions and conflicts in the developing child. This point is argued in a cogent manner in the discussion by the psychoanalyst Marjorie Barnett.

What can be said about the volume as a whole as a representative but certainly not a comprehensive sample of what psychoanalysis has to offer the psychiatrist who cares about what psychoanalysis can contribute to the field and to knowledge generally?

First, the articles in this volume, although differing in importance, are all serious and scholarly contributions and can be taken as a tribute to George Pollock's final year as chairman of the editorial committee. Beyond that, the articles are devoted mostly to applied psychoanalysis and theoretical and developmental issues; clinical material is very sparse. Discussion of the strengths and weaknesses of psychoanalysis as a method for treating patients is almost nonexistent, and, from my observations, this lack is also found in the current psychoanalytic literature generally. The articles in the volume do not include discussion of the biological and genetic discoveries that have significantly altered our understanding, not only of many forms of psychopathology but also of some of the issues discussed in the book, and no effort is made to integrate these findings into psychoanalytic thinking. As to the several essays that attempt a psychoanalytic exegesis of creative activity, there is no doubt that psychoanalysis has made and continues to make an important contribution by exploring the unconscious roots of creativity. However, this contribution is not enhanced by a narrow and rote reduction of the productions of creative persons to their putative origins in infantile sexuality.

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The Technique and Practice of Listening in Intensive Psychotherapy, *by Richard D. Chessick, M.D., Ph.D. Northvale, N.J., Jason Aronson, 1989, 266 pp., $27.50.*

This book is extraordinary. The author is a prolific contributor of worthwhile practical and educational psychoanalytic material to our literature. He is a dedicated teacher and psychoanalytic practitioner. With convincing clarity and expedient organization, the book directs our attention to effective multimodal overtures to the patient.

In the introduction, Chessick states, "This book is intended to facilitate the teaching and learning of psychoanalytic listening," and he reaches this goal successfully. The book consists of eight chapters. The first succinctly explains Freud's basic principles and his technical advice for listening, emphasizing "evenly suspended attention" with rejection of anything in particular and note-taking. Dr. Chessick declares his orientation: "A psychoanalytic model is the only acceptable one if we want thoroughly and deeply to understand our patients." Moreover, "one neglects Freud's [orientation] at one's peril."

In chapter two, "Listening Stances," Chessick elucidates five listening channels. The first, the psychoanalytic drive/conflict/defense orientation, is the fundamental theory and therapy to understand patients. The second channel is the object relations approach, which is linked to Melanie Klein and Bion's recognition of earliest projection and introjection fantasies expressed in the transference. It is the function of the therapist to make unacceptable fantasies acceptable and to refrain from judgment and the like. The third channel is the phenomenological approach, defined as "being in the world" and taking the patient's utterances at face value. The fourth channel, self psychology, founded by Kohut, emphasizes empathic failure in dynamics and therapy. (Chessick's demonstration of the method is presented later, in chapter six, where he evaluates Kohut's patient Mr. Z.) The fifth channel is interactive therapy. Here the effects of countertransference in the "here and now" are considered, increasing thereby our understanding of the pre-oedipally damaged patient. Rather than explanation, the patient needs experience in the interactive dyadic situation. Chessick states that channels other than psychoanalysis, if used exclusively, are considered by many psychoanalysts as defensive against infantile sexuality, aggression, and the oedipal complex. These supplementary channels are to be used in reaction to patients' utterances and are not to be imposed on them. Moreover, they are to be used interchangeably as the occasion requires.

Illustrative cases are presented with verbatim reports and annotative critical remarks by the author in accordance with the five channels. In chapter three, "Listening to the Psychotic Patient," Binswanger's treatment of Ellen West, who committed suicide after discharge from the hospital, is presented. This case is a dramatic illustration of listening with one channel, a "blatant mishandling of a patient." Interactively, by means of projective identification and counteridentification, the patient seemed to "infect her caretakers with her despair," leading to acting out the destructive countertransference of hopelessness.

Chapter four, "Listening to the Borderline Patient," deals with Basche's treatment of Miss Banks, which reveals a collusive avoidance of infantile sexuality. Through denied responsiveness, patients with borderline disorder, fearing rejection, protect themselves from the need for love. Tolpin's case of Louisa A. is cited as illustrating the limits of psychoanalytic listening. Chessick addresses the responsibility of the therapist to stay with the patient in long-term therapy for the development of internalized controls before the patient is ready for interpretation.

In chapter five, "Listening to the Neurotic Patient," Freud's seven therapeutic sessions with the Rat Man are discussed. Chessick notes that Freud's therapeutic method was at times a "far cry from the mental opaque mirror" he advised. He was authoritative, mailed a card to his patient while on vacation, lectured on psychoanalysis, was supportive, and even promised the Wolf Man a gastric cure.

Chapter six, "Listening to the Narcissistic Patient," concerns the controversial work of Kohut with Mr. Z., in which it is claimed that empathy was curative in a second analysis. It is believed that self psychology in this case reflected a collusion with the patient to flee from oedipal conflicts.

In chapter seven, "Listening to the 'Difficult' Patient," Chessick presents his annotations on a case presentation and discussion by Arlow. This chapter describes the countertransference of the therapist when the patient torments, teases, manipulates, and challenges in therapy.

Chapter eight, "Learning to Listen," is the final chapter and is an inspirational appeal by Chessick for therapists to prepare appropriately for therapy. Although some therapists are gifted with intuition for treating patients, methods can be learned through personal analysis and supervision and through failures to develop the capacity to use all listening channels appropriately.

Lest we forget, the patient is seeking help in overcoming the pain of unconscious conflicts. The psychoanalytic method is stark, unsupportive, and demanding; the tools of abstinence, anonymity, and interpretation expose the primary process. The reactive urge of the patient is to flee, and the therapist's objective is a holding preparation for analysis. This is best attained through the channels eloquently recommended by Chessick. All mental health professionals will find this book a joy to read and a source of immense practical knowledge. An extensive bibliography and a workable index are provided.

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CHILDHOOD AND ADOLESCENCE

The Lost Childhood, *by Yehuda Nir. Orlando, Fla., Harcourt Brace Jovanovich, 1989, 256 pp., $19.95.*

This book is written by a child psychiatrist who has captured in his own autobiographical memoir a devastating period in world history through the eyes of a boy struggling to survive. Yehuda Nir, born in Poland 60 years ago, was 9 years old when the Nazis invaded his country and he was forced into a horror that, for most human beings, would be incomprehensible. His book is impossible to put down. It is vivid and eminently readable. It grips you like a novel and, because it is the truth, the horror is even more impossible to believe.

There are several things that are difficult to comprehend when one reads this book. The most incredible aspect is how young Yehuda Nir was at the time that all of this took place. Those of us who do child psychiatry or have watched young children grow and mature in a normal environment realize how immature 9-year-olds are. Yehuda Nir grew up fast in a world that not only must have been overwhelming in its cruelty and barbarism but that also forced him to solve problems and deal with issues which most of us, no matter how old, have never experienced.

The book opens with a brief description of the comfortable middle-class home from which the family was evicted when the Nazis invaded Poland and a brief description of the trials and difficulties that all of the family members had to endure. The death of his father and the miraculous survival of Yehuda, his sister, and his mother provide insight into how human beings address the basic survival tactics necessary with total disregard of the greater geopolitical forces and how important small things are in the excruciating stark realities on which matters of life and death rest.

Reading this book, each time Dr. Nir and his family went through a narrow escape from what appeared to be certain death, I breathed a sigh of relief and thought that now I would read about their escape to Israel, where they were finally able to go after the war. But each time there was another difficult, painful experience to endure. The events are told in a frank, penetrating, incisive narrative style.

This book has been critically acclaimed by a number of reviewers, including some who have been writing about the Holocaust for years. It was named as the critics' choice in the *New York Times Book Review* and has received some other noteworthy accolades.

Yehuda Nir and I first met on our first day of residency. Very early on he demonstrated his intellect, sharp wit, intuition, and sensitivity. For his fellow residents he was someone who could be relied on for incisive and telling accuracy. The same characteristics that we discovered in him during those years are reflected in this book.

Psychiatrists and other mental health professionals should read *The Lost Childhood.* We all know that life experience plays a substantial role in the growth and development of a psychotherapist. To do good therapy one must be rooted in reality and have a capacity for empathy as well as a sound philosophy of life that grows out of experience. It was important for Yehuda Nir to tell his story, not only for himself but for all of us, as a testimony to the resilience of a remarkable boy who survived to become an honored colleague.

For me this book is an important affirmation of the human spirit—the story of a little boy whose ingenuity and will to live continually snatched victory from the jaws of defeat.

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The Child in Our Times: Studies in the Development of Resiliency, *edited by Timothy F. Dugan, M.D., and Robert Coles, M.D. New York, Brunner/Mazel, 1989, 240 pp., $27.50.*

At the end of her chapter in this volume, "Defying the Voice of Doom," Stella Chess suggests that the stories of individuals who succeed despite adversity might better be told by novelists. She names George Eliot and quotes from *Middlemarch.* (She could equally have called on Dickens or Steinbeck.)

Indeed, this book could well have done with a single author to consolidate the data and to present the case descriptions that explicate the concept of invulnerability. Conceived during what must have been an exciting conference with the book's title at the Cambridge Hospital, the chapters suffer from their separateness. The material is abundant but, at times, overlapping, in setting forth the characteristics of individuals who demonstrate an ability to rise above early handicaps.

Does resilience come, as Chess states, because of adolescent abilities to develop distance "from noxious familial onslaughts," or is it the capacity to work and engage in alternate social roles, as described by Vaillant?

Individual chapters have true merit. Demos's opening chapter uses Sander's 30-year study of children and families to set a dynamic tone that depends on long-term data as well as an understanding of family relationships and environments. Demos also poses a question that the entire volume struggles to answer—Do highly resilient children remain so?

Two succeeding chapters set forth novel concepts of the unique moral forces within children that enable them to succeed; unfortunately, such capacities are not highlighted in other essays. There are, however, excellent descriptions of street children, children who survive alcoholic families, and a special group of children—those stressed by chronic physical disabilities. In all instances there are clear pictures of the impact of the family on the child as well as the ability of the child to use or to create distance from such impacts.

The most integrative writing is that of the editor, Timothy Dugan, who uses the book's data (as well as the iterative references to Garmezy, Rutter, and Winnicott) to put resiliency in the context of action and acting out. Noting that the adaptive capacity to act in relationship to others may result in "provocation or annoyance," Dugan describes a key issue in therapy as well as in studies of outcome: Are resilient children also the subsequent provocateurs of society? The text hints at this, but it needs further documentation. Acting out may well be protective to the individual; is it equally helpful to others? In view of Dugan's criteria, it would be interesting to know whether the "gamins" of Columbia, described by Felsman, grow up to be political leaders or drug lords.

Dugan's chapter is not placed as a summary, but it does bring forth many of the common traits that enable some children to rise above seemingly noxious beginnings. The various authors agree that it certainly helps to have usable intelligence, a warm parent or mentor, special talents, and a drive to use these assets.

While such capacities are not universally available, the timeliness of this book is manifest in its opportunity to assist us in a period of growing homelessness and seeming increase in the abuse of children. We will continue to need the extension of the long-range studies described here (as well as others referred to). We could also profit by a more critical—even if idiosyncratic—editorial organization of the various data.

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The Abandonment of Delinquent Behavior: Promoting the Turnaround, *edited by Richard L. Jenkins and Waln K. Brown. New York, Praeger, 1988, 226 pp., $39.95.*

As one might possibly surmise, this book is devoted to the subject of delinquent young people who straightened out. It is meant, I think, as an antidote to the pessimism that pervades the literature on delinquent and/or antisocial adolescents and young adults. (Not all antisocial people have been formerly adjudicated as "delinquent," nor, in actuality, do all youngsters who commit an act judged delinquent have antisocial personalities; hence, the terms are not synonymous.)

As an edited volume, the book is an interesting potpourri of literature reviews and a few long-term follow-up studies, first-person accounts by former delinquents who "made good" giving their thoughts regarding the evolution of the turnaround, a couple of theoretical papers on the whys of delinquency, and several papers discussing interventions (juvenile court adjudication, training schools, etc.).

Specifically, the first-person accounts by Robert E. Thornton, M.S.W., and Warren Rhodes, Ph.D., men with histories of delinquent behavior in adolescence who describe their turnaround, provide an implicit and explicit message. The explicit message is that help helps. The implicit message is that brains and, finally, learning from experience that getting into trouble is not fun and can be avoided are vital. The inability of certain people to learn from experience, although not part of current diagnostic criteria, is one of the more frustrating (for the helpers) aspects of dealing with people who are delinquent or antisocial.

Another notable chapter, by Gerard E. Nelson, M.D., and Richard W. Lewak, Ph.D., is a brief readable synthesis of attachment theory and its contribution to the understanding of delinquency. Finally, the chapter by David P. Farrington, Ph.D., Bernard Gallagher, Lynde Morley, Raymond J. St. Ledger, and Donald J. West, M.D., updating the well-known Cambridge Youth Study, provides some important data. Although their data suggest that by age 32 the amount of delinquent behavior has diminished (the "burning out" of antisocial behavior is a well-recognized phenomenon), those who were staying out of trouble were not necessarily positive contributors to society. Their existence often seemed marginal at best.

I had intended to read this book only selectively, but I found it sufficiently interesting to read from cover to cover. The question of why some youngsters can survive devastating environmental and family difficulties that "cause" others to become delinquent, psychotic, or depressed is a compelling and, as noted by the editors, understudied one. My conclusion after reading these selections was not specifically addressed by any of the contributors and is relevant insofar as the recommended audience for this book is concerned. That is, the impact of psychiatric disorder on delinquency was never considered. Those who "survived," so far as I could tell, were not additionally handicapped with attention deficit hyperactivity disorder, severe learning disabilities or mental retardation, schizophrenia, substance abuse, or organic brain syndromes. The closest the book came to this context was the study by Gene M. Lutz, Ph.D., and Kriston Baughman, which concluded that boys with greater aggression, less education, and from families with less education were more likely to have continued problems.

Unfortunately, most of us in the mental health profession who become involved with delinquents are asked to consult on the question of mental illness over and above the behavior disorder itself. Thus, the interventions and outcomes of people without concurrent mental disorders or with unknown disorders may not be of as much interest to a psychiatric readership. On the other hand, for those professionals who work with the courts or in residential facilities, this volume provides some interesting insights.

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Relationship Disturbances in Early Childhood: A Developmental Approach, *by Arnold J. Sameroff and Robert N. Emde. New York, Basic Books, 1989, 255 pp., $24.95.*

There has been a quiet revolution going on in the field of child development. Development is no longer seen as unfolding within the child while the environment merely tries to respond to the process. This individualistic perspective has been supplanted by an interactionist position in which the development of the self is the result of a dynamic, reciprocal relationship between biological givens and life experiences. This cohesive, well-written book not only contributes to the revolution but assures that this dramatic shift is now audible in the field of psychiatry.

This volume originated from the interactions and discussions of a special project group at the Center for Advanced Study in Behavioral Sciences. The multidisciplinary group of eight prominent scholars (Sameroff, Emde, Daniel Stern, Alan Sroufe, Thomas Anders, Arthur Parmelee, Herbert Leiderman, and David Reiss) represent the fields of developmental psychology and psychiatry. They collectively derived the constructs presented and, thus, have produced an integrated work. Its focus is on relationship disorders, their classification, and how disorders of early childhood may serve as a basis for relationship disorders in later life. The text challenges the reader with a bold conceptualization of the infantcaretaker dyad, an external relationship, as dependent on and generative of internal representations. Similar to Winnicott's often quoted, "There is no such thing as a baby," the authors argue effectively that early childhood psychiatric disorders should be classified as relationship disorders.

This position raises questions: Where do relationship patterns reside? What gives them their continuity? How do disorders in relationships become disorders in individuals even when the relationship is no longer active? The authors tackle these questions, enriching the field of developmental psychopathology—relevant for general psychiatrists—while offering a taxonomy of relationship disorders for those specializing in the early years. The authors' focus is the influence of relationships in the construction of the self. They are respectful, however, of biological aspects of psychiatric practice. They view physical illness, temperament, parental vulnerability, and life events as all part of the equation of the self and serving to influence how a child forms and maintains relationships.

The book is divided into three sections: Development, Disturbance, and Context. Several exciting themes serve to integrate these sections. Relationship disorders are described in a spectrum of increasing severity—perturbations ("normal" frustrations) to disturbances to disorders (more than one area of development or relationship affected). Regulatory aspects of relationships, analogous to physiological regulation of internal states, are emphasized, and the family's overregulation and underregulation of a child's developmental experience are used as examples. The science of psychodynamics is advanced by a vigorous attempt to understand the mental mechanisms of how life experience gets encoded and how this internalization affects future life events.

We have little to criticize. The relationship of the authors' work to extant views of development and psychopathology is indirect and muted. Broadened discussion of how this work relates to self psychology, object relations theory, biopsychosocial psychiatry, and systems theory would have been challenging. Some may find the work too theoretical and desire more clinical material.

This remains a significant contribution. We hope the apparently limited focus—infancy and early childhood—does not obscure its relevance to the entire field of psychiatry. This book is not merely about an interesting nosological issue, the classification of relationships. Rather, the authors have made a major contribution to the field of human development and psychiatry. Psychiatrists will find the mechanisms of psychopathology elucidated; psychotherapists will appreciate the descriptions of self formation; family therapists will have their perspectives on systems enriched. Although some background in development would be helpful, we believe any student of human behavior should read this work.

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Child and Adolescent Psychopathology and Involuntary Hospitalization: A Handbook for Mental Health Professionals, *by Tony D. Crespi. Springfield, Ill., Charles C Thomas, 1989, 124 pp., $31.75.*

After having survived and been rehabilitated for a brutal beating by an inpatient adolescent, Dr. Crespi has given much thought to the issue of psychiatric treatment of children and adolescents. He has written a clear and concise manual that details the issues surrounding psychiatric treatment of adolescents. Because "psychiatric treatment for young people consumes a diverse range of specialties and professional subgroups" and "the psychiatrist actually occupies the smallest piece of the pie," this book is intended as a comprehensive reference for psychologists, counselors, social workers, and other mental health professionals. Although the title of the book implies a discussion of child and adolescent issues, the bulk of Dr. Crespi's work focuses on adolescent psychopathology and involuntary hospitalization.

There is a rich history of treatment of adolescents aptly documented in the first parts of the book. For instance, although the first mental hospital in the United States was opened in 1852, the first all-adolescent unit was not established until 185 years later at Bellevue Hospital. About two-thirds of all patients were court referrals, and the ward milieu was aggressive and destructive. Custodial and restrictive care were seemingly the only ways staff could maintain control. In this historical light, Dr. Crespi's comments on the recent upsurge in adolescent hospitalizations and continued violence are disturbing; large-scale follow-up studies assessing treatment efficacy have not been attempted.

The chapter on commitment procedures is general and well written. Although each state has specific guidelines, the author does an excellent job of outlining what parents', therapists', and patients' rights are in the process. It is a chapter that especially can be read by families, as Dr. Crespi suggests.

The chapter on medication used with young people is not detailed enough for medical practitioners and serves to clearly define the book for nonmedical personnel. The most interesting chapters, however, are devoted to an explanation of adolescent psychopathology, paying particular attention to behavior disorders, suicidality, use of restraints, and seclusionary procedures. These latter points are discussed in a most useful manner, raising questions as to the long-term effects on the adolescent who is coping with mental illness. Again, Dr. Crespi calls for a studied approach to answering this question.

Completing his analysis of adolescent hospitalization and psychopathology, Dr. Crespi ends the book with an enlightened view of discharge planning. He advocates careful planning in the discharge process and attention to treatments and preparations that will keep the patient out of the hospital and integrated into the community.

Overall, this book is exciting to read because of the activism evident in Dr. Crespi's writing style. From the very beginning he draws the reader in as he describes his own experience with a violent patient. The beating and the rehabilitation only hinted at remind the reader that these patients must be taken seriously.

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AGGRESSION

Wartime: Understanding and Behavior in the Second World War, *by Paul Fussell. New York, Oxford University Press, 319 pp., $19.95; $9.95 (paper).*

It can be refreshing to turn from the pages of our professional literature and observe human nature through the eye of a keen, unrelentingly honest, and articulate "natural psychologist," unfettered by codes, axes, or statistical analyses. That is a portion of the pleasure we can continue to take in

Freud, and much of the delight one may find in the writing of Paul Fussell.

Fussell, a professor of literature at the University of Pennsylvania, has, in addition to his academic writings, produced a steady output of iconoclastic, irreverent books and essays. His concern—broadly speaking—is the human condition. His work is wide-ranging: from the hilariously unorthodox and deadly discerning *Class: A Guide Through the American Status System* (1) and the controversial but compelling *Thank God for the Atom Bomb and Other Essays* (2) (Fussell's one-time front-line foot soldier's defense of the bombing of Hiroshima and Nagasaki) to his award-winning study of World War I, *The Great War and Modern Memory* (3).

In his most recent work, *Wartime,* Fussell uses techniques advanced in *The Great War* to examine popular songs, poems, literature, letters, and memoirs to identify and understand the changes in human thought and feeling, individual and collective, that transpire in wartime. In the present work Fussell turns to the war and the people he knows firsthand, Americans and Britons during World War II.

Fussell begins with the psychological civil defense engaged at the beginnings of all wars: denial on a mass scale. The general public hardly contemplates the horror of actual combat. Instead, we assure ourselves the war will end quickly in an easy victory with few casualties. Fussell compares the early days of the Civil War, when elegant ladies brought their evening dresses to the Battle of Bull Run for the post-battle ball that was never held, to the beginning of World War II, when Luftwaffe pilots who crashed in the English countryside were buried with full military honors.

As the realities of wartime transcend denial, a collective fear replaces it, a fear that Fussell argues has been lost to selective memory. Fussell recounts fear on the home front and fear at the battle front. Fear, he tells us, so tormented London anti-aircraft gunners that they could not wait for incoming planes to fly close enough for visual identification. They fired so unselectively that Allied pilots self-protectively avoided flying over London.

Fear leads us to ascribe evil intentions to the inevitable, random accidents of wartime. Human motives are projected onto happenstance. So espionage must lie behind otherwise inexplicable failures: saltpeter rather than exhaustion and anxiety saps soldiers' libidos; gremlins haunt ill-fated bomber crews.

Rampant fear sows rampant rumor, which sustains hope and offers magical outcomes. Even the most awful tale remains a respite from reality, and erroneous news is more exciting than silence. The prisoner of war hears rumors of his own wishes: imminent liberation or prisoner exchange and, inexplicably, that Henry Ford is giving every POW a brand new automobile.

Through its power, rumor itself naturally evolves into a weapon of war. Fussell quotes the methodology of the Office of Strategic Services (the OSS, predecessor of the CIA) for disseminating disinformative rumors among the enemy. This advice bears the earmarks of dogged experience:

> 1. Tell the story casually, and don't give yourself away by being overanxious to launch your rumor.
> 2. If the lowdown is especially hot, tell it confidentially.
> 3. Never speak your rumor more than once in the same place. If it is good, others will repeat it.
> 4. Tell it innocently, and don't disclose any source that can readily be discredited.

The favorite OSS rumors for the two theaters of war were, in Europe, that Hitler was epileptic and/or insane and, in Asia, that native girlfriends of Japanese soldiers were slowly poisoning their food.

The waging of war has its own psychology, as we learn from General George Patton, who cautions that "reports by wounded men are always exaggerated and favor the enemy." Likewise, reports of events after nightfall are per se unreliable. Patton's psychology of leadership: in cold weather never dress more warmly than the troops. When visiting the front, drive up in a jeep. Fly back. Never be seen heading for the rear.

Fussell does not view such psychological warfare as a limited aspect of the war. He draws a larger picture of the Allied war effort—the propaganda, disinformation, misinformation—as an exercise in deception, required to generate a moral fervor equal in motivating force to the power of the Emperor over the Japanese and *Fuhrer und Vaterland* over the Germans. Fussell claims the Axis had a clear purpose: to conquer. The Allies had a dirty job: to stop the Axis and go home.

Although not often expressly stated, this is not an original thesis. Frank Capra, in directing the *Why We Fight* documentary series for the war effort, divined that the most effective method of inspiring his viewers was to show them not what they were fighting for but what they were fighting against. Propaganda footage of Axis leaders and scenes of brutal aggression and war were more compelling than anything Capra himself could record on film.

Fussell's statement that the events of the war, "being inhuman, have no human meaning," has ignited a firestorm of criticism. Fussell has been accused of suggesting that the Allied role in World War II was immoral and that the war should not have been fought. *Wartime,* with its relentless criticism of the illusions and distortions that accompany even the most noble of wars, easily invites the hostility that greets messengers who bring bad news, particularly in time of war.

Fussell, who was wounded fighting in France, neither doubts the necessity of the war nor regrets the outcome. He regrets casualties that are not usually thought of as such: casualties in understanding, thought, and emotion. Like the iconoclast he is, he probes without regard for whose pride might be punctured. In his earlier essay, "Thank God for the Atom Bomb" (2), Fussell made the brazen suggestion that those Americans who would second-guess the decision to drop atomic bombs on Japan are an elite group, alienated from the socioeconomic class who would have continued to fight the war had the bombs not ended it.

Such pointed and unsettling ideas are vintage Fussell. Time and again, Fussell, like Freud, dares to disturb the sleep of the world. His insights, although often discomforting, are, like many discomforts, incentives to reexamine and think anew. Fussell's book on the psychology of wartime—a psychology that, thankfully, ever fewer of us know firsthand—expands one's understanding of human thought and behavior. In psychiatry we can ask little more of any text.

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The Painful Field: The Psychiatric Dimension of Modern War, *by Richard A. Gabriel. Westport, Conn., Greenwood Press, 1988, 200 pp., $39.95.*

Unfortunately, this book is written in a dry, repetitive style that makes its reading somewhat boring. There is no question that Richard Gabriel, an Army Intelligence officer turned academician, knows his subject, as evidenced by the fact that he has written at least 18 books on war in the last few years. One of them, *No More Heroes: Madness and Psychiatry in War* (1), is of particular interest to me because it seems to be a more compact and readable version of *The Painful Field.* The earlier book has the same information, the same warnings, and the same conclusions. In both books we read mind-boggling items such as that modern armies have more machines of destruction at their disposal than any other armies in history, that "on the first day of fighting both sides would be able to engage almost 20,000 modern main battle tanks, and after 30 days, the number of tanks on both sides would increase to 66,000," that in the Arab-Israeli War "both sides suffered losses of 50% in men and equipment in less than two weeks of fighting, that "even assuming . . . best case scenarios, the number of men killed and wounded in a central European battle will approximate two million on both sides if the battle lasted only two weeks."

Gabriel also writes about personal and ethical issues of tremendous importance, reminding us that we are a fortunate nation, only lightly touched by modern war with relatively few casualties, no civilian deaths, and no mass destruction of property compared with other nations. He also informs us about Soviet and American military psychiatry, attempting to condense history and clinical issues into about 100 pages with limited success.

The final chapter of *The Painful Field,* which concerns the future of military psychiatry, touches on the future of battlefield psychiatry and more specifically on the "chemical soldier." Gabriel writes that "without chemical assistance the human psyche can no longer withstand the stress of modern war without seeking refuge in insanity, creating the necessity to find a chemical compound that will prevent or reduce anxiety while allowing the soldier to retain his normal and vitally needed acute levels of human awareness." Gabriel assures us that the search for these chemicals is already underway in the military research laboratories of the major armies of the world.

Are we, the psychiatrists of this world, collaborating in this research? Have we lost our minds and become participants in the creation of killing machines? Are we ready to participate in the destruction of humanity? Answering these questions, I would like to quote from the Nobel Prize acceptance speech of Gabriel García Márquez: "Faced with this awesome reality that must have seemed a mere Utopia through all of human time, we the inventors of tales who will believe anything, feel entitled to believe that it is not yet too late to engage in the creation of the opposite Utopia. A new and sweeping Utopia of life, where no one will be able to decide for others how they died, where love will prove true and happiness be possible, and where the races condemned to 100 years of solitude will have, at last and forever, a second opportunity on earth." I hope that the inventors of tales would convince us that this Utopia is far better than the one coming out of this book called, appropriately, *The Painful Field.*

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Reprints of Book Forum reviews are not available.

Letters to the Editor

Dantrolene in Lethal Catatonia

SIR: Stauder's "lethal catatonia" (1) remains a rare but dramatic problem because it is a highly life-threatening disorder (2). Early interventions with ECT or steroids constitute the only sufficiently tested therapies (3). Since neuroleptic malignant syndrome has sometimes been considered to be an iatrogenic variant of lethal catatonia (2, 3) and dantrolene appears useful in neuroleptic malignant syndrome (4, 5), we decided to treat two patients who had lethal catatonia with this drug.

Ms. A, a 57-year-old woman with bipolar disorder diagnosed according to *DSM-III-R*, was treated with imipramine for a depressive episode. In a few days she became extremely irritable and refused food and water. Within 2 days after hospitalization, she manifested mutism, psychomotor retardation, generalized muscle hypertonicity, and fever. In the following 24 hours the clinical picture worsened: stupor alternated with intense agitation, and Ms. A believed herself to be dead. Furthermore, her fever stabilized at 40 °C, her blood pressure became unstable, and hypernatremia, hypokalemia, hypocalcemia, hyperazotemia, urinary retention, dynamic ileus, and a slight lung infiltrate appeared. The addition of acetylsalicylic acid (1 g i.v.), noraminopyrine (1 g i.m.), ampicillin (3 g i.v.), and amikacin (1 g i.v.) and rehydration with chilled intravenous balanced fluids were unsuccessful in the following 48 hours. Dantrolene (75 mg i.v.) was then administered, and in 24 hours Ms. A's temperature, diuresis, muscle tone, and blood pressure returned to normal, and the psychopathological picture improved; she accepted food and became sufficiently collaborative. After 9 days of decreasing doses of dantrolene (up to 25 mg p.o.), the patient was discharged.

Ms. B, a 63-year-old woman with a *DSM-III-R* diagnosis of paranoid schizophrenia who had not taken neuroleptics for the past 7 years because they produced severe extrapyramidal side effects, began to take diazepam (18 mg/day p.o.) during a residual phase of her illness. In a week she became progressively agitated, verbalized nihilistic delusions, and refused both liquid and solid foods. Within 2 days after hospitalization she had a fever (39.7 °C), generalized muscle hypertonicity, marked fluctuations of both blood pressure and heart rate, slight lung infiltrate, hypernatremia, hypokalemia, increase in ESR, and neutrophil leukocytosis. Despite the addition of ampicillin (3 g i.v.) and acetylsalicylic acid (1 g i.v.) and rehydration with chilled balanced fluids, her temperature rose to 40.7 °C, and extreme agitation and stupor alternated during the following 24 hours. Dantrolene (75 mg i.v.) was administered, and in 48 hours her muscle hypertonicity substantially decreased and her temperature fell to 38.3 °C. The phases of motor agitation and stupor disappeared, the delusions subsided, and Ms. B agreed to eat and drink. Dantrolene was continued for 7 days, and after 14 days the patient was discharged.

The chronological link between administration of dantrolene and recovery from lethal catatonia could have been coincidental. Nevertheless, evidence that in lethal catatonia the drug reduced the same symptoms that it positively affected in neuroleptic malignant syndrome sufficiently supports the inference that dantrolene exerted therapeutic activity. Further, the consensual reduction in the psychopathological picture and the physical symptoms suggests that dantrolene had central effects as well. Whatever the case, further experimentation with dantrolene in lethal catatonia appears justified.

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An Adverse Reaction to L-5-Hydroxytryptophan

SIR: The drug 5-hydroxytryptophan has been used for treatment of depression (1) and also as a tool to investigate the role of the serotonergic system in the pathogenesis of affective disorder (2) and schizophrenia (3). Some physical and psychological adverse effects of the drug have also been described (4). We report here a severe adverse reaction to 5-hydroxytryptophan, not reported so far, in a depressed patient with atopic dermatitis.

Mr. A, a 30-year-old man, presented at our hospital with depressive symptoms of 1 month's duration and was diagnosed as having major depression with melancholia according to *DSM-III-R*. After giving written informed consent, he was included in our study, which entailed measurement of serum cortisol response to oral 5-hydroxytryptophan. The patient had a chronic atopic dermatitis with thickened and coarse skin. There was no history of drug reaction, and he had not taken any drug in the past month. His hematological, biochemical, liver, and kidney functions were normal except for a raised eosinophil count of 7%.

After an overnight fast, Mr. A received 5-hydroxytryptophan, 3 mg/kg orally, in a non-enteric-coated capsule, followed shortly by a light breakfast (a slice of bread with jam) to avoid nausea. Approximately 90 minutes after taking the drug, he experienced generalized itching and became restless. Soon he complained of dizziness, blurring of vision, and difficulty in breathing. His appearance was flushed and his pulse increased from 80 to 100 bpm, but no change in blood pressure was recorded. Cyproheptadine, 8 mg orally, was given immediately. The patient gradually recovered in about 2 hours.

The observed reaction is highly suggestive of a reaction to 5-hydroxytryptophan because of the temporal relationship with its administration and Mr. A's response to the serotonin antagonist. The patient was not taking any drug or food rich in serotonin or its precursor. Exogenous 5-hydroxytryptophan is expected to raise serotonin levels in the body, which can explain the effects seen in this patient. However, the possibility of an immune-mediated anaphylactoid reaction cannot be ruled out, especially since this patient was suffering from atopic dermatitis, and such patients are known to be unduly sensitive to allergens (5).

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Restraining the Violent Pregnant Patient

SIR: Because of the infrequent use of restraints to control violent behavior of hospitalized pregnant psychiatric patients, this intervention often causes intense discussion. Muqtadir et al. (1) stated that restraints were never used for fear of provoking maternal injury. Chang and Renshaw (2) appear to endorse medication rather than restraint for agitated pregnant patients because restraint might "aggravate the patient's distress." We could find no descriptive literature on the use of restraints for pregnant patients. We would like to present the case of one such problematic patient.

Ms. A was a 21-year-old obviously pregnant woman admitted to the psychiatric ward on a police officer hold. She had thrown a brick through her boyfriend's window and threatened to stab herself in the abdomen. There was an extensive history of drug abuse. She had been treated with a combination of perphenazine and amitriptyline, which had been stopped by her physician when she became pregnant. On the ward she was frequently hostile, misinterpreting the intentions of others and insisting that one staff member was Satan. There was no evidence of delirium. She was placed in restraints for 24 hours after throwing objects at the nursing staff. After a few days in the hospital, her mental status cleared and she was released by the court. Ms. A was admitted to the obstetrics ward 9 days later because of complications secondary to cocaine use. She made repeated threats toward the staff, tried to leave the hospital, and threatened to hurt herself. She had ideas of reference and paranoid delusions. She was placed on a second court hold and transferred to the psychiatric ward. She required restraints to keep her from leaving the hospital or harming the staff. Again, she was released by the court.

The clinician is faced with the dilemma of having to choose between interventions with complex and occasionally unknown risk-benefit ratios. If a patient presents with dangerous, out-of-control behavior that does not respond to verbal intervention or less restrictive means, such as isolation in an unlocked or locked seclusion room, we would recommend avoiding medications and considering restraint until the duration and etiology of the behavior are known. Also, possible disposition and compliance with follow-up play a role in intervention decisions. The impact of medication on pregnancy, mother, and fetus are well described (3).

Historically, restraints have been used during obstetrical delivery, but this practice has been largely abandoned. It is considered dangerous to restrain second- and third-trimester patients on their backs because of obstruction of the venous return to the heart and development of supine hypertensive syndrome (4). A patient requiring restraint should be placed on her left side or be restrained with a pillow, raising the left hip. Frequent change of position is helpful in reducing partial inferior vena cava obstruction as well as any dependent edema.

We favor considering restraints in emergency situations, which allows reflection on the risks and benefits of medication. We believe this is a lesser risk and a more easily reversible decision. Clearly, more research in this area is warranted.

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Exaggerated Sensitivity to an Organophosphate Pesticide

SIR: Although it has been reported that organophosphate pesticides induce psychiatric symptoms—most notably, depression, psychosis, and anxiety—in chemical workers (1) or after intentional overdose, little has been written about the toxic effects of "routine" exposure in vulnerable individuals. Roueché (2), in a magazine article, reported on a woman whose idiosyncratic sensitivity went unrecognized by physicians, heightening her sense of isolation and despair. We present a case report of a patient with a long history of recurrent depressions.

> Mr. A, a 64-year-old retired attorney, had been treated with a variety of mood-altering medications with limited success, due largely to his intolerance of side effects, even at low doses. Nevertheless, he had maintained reasonable mood control through psychotherapy, stress management, and regular exercise.
>
> Following termite treatment of his house with the organophosphate chlorpyrifos, Mr. A noted a foul smell and shortly thereafter complained of severe abdominal pains, nausea, headaches, difficulty breathing, fatigue, and irritation of the eyes, nose, and throat, accompanied by anxiety and irritability. These symptoms have continued to plague Mr. A for the 2 years since the termite treatment whenever he is in his home and for many hours thereafter, and the irritation of his mucous membranes over the years has been validated by examination. His search for alternative lodgings whenever possible has created considerable stress but does help relieve the toxic symptoms.
>
> Anticholinergic antidotes have offered minor relief. He is currently taking 2 mg of lorazepam at night to help him sleep and has tolerated this medication reasonably well. He has met with considerable skepticism about the authenticity of his symptoms both inside and outside the medical profession.

The symptoms reported by Mr. A are well-documented effects of organophosphate intoxication (3). However, they have been unusually severe and long-lived in his case. He has shown evidence of sensitivity to other environmental chemicals, for example, those emanating from new furniture and carpets, as well as to a variety of psychotropic medications.

Patients with extreme chemical sensitivity such as Mr. A offer the following lessons for psychiatrists. 1) We may be in the best position to detect and validate symptoms of intoxication from "safe" chemicals that do not appear to affect most people. 2) Like the oxygen-sensitive canaries that miners used to detect dangerously low levels of oxygen, these hypersensitive individuals might be signaling to us toxic effects experienced by far larger numbers, although to a lesser degree. The psychiatrist can act as a sentinel to alert public health officials of such cases and dangers. 3) Environmental toxins should be considered as potential triggers of apparently "idiopathic" exacerbations. Patients who are intolerant of psychotropic drugs and other chemicals may be prime candidates for such consideration. These patients should be encouraged to avoid the harmful chemicals, and in some cases antidotes may be available, for example, anticholinergic drugs for organophosphate intoxication. 4) For the researcher, this abnormal sensitivity raises the question of mechanism. It has been hypothesized that patients with depression are hypersensitive to the effects of acetylcholine (4), the very chemical whose breakdown is retarded by organophosphate pesticides. Such vulnerability to the effects of acetylcholine might account for both environmental hypersensitivity and the endogenous tendency to become depressed.

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Abuse of Ethyl Chloride

SIR: I would like to call attention to the emerging use and abuse of the volatile gas ethyl chloride, now widely available and sold under the names "Ethyl Gaz" and "Ethyl Four Star" in the Chicago area.

Use of ethyl chloride was not included in a major review of volatile substance abuse by Ron (1) in 1986. Two case reports can be found in the literature, one by Nordin et al. (2), involving a 52-year-old man employed in the chemicotechnical industry, and one by Hes et al. (3), involving a 26-year-old woman. Both case reports documented a complex syndrome with psychological and neurological symptoms after daily use of ethyl chloride over many months, with full recovery after a period of abstinence during inpatient hospitalization.

Use of this substance came to my attention when it was among the drugs of choice of a patient of mine who sought inpatient treatment for alcohol addiction. This 45-year-old homosexual man had previously used amyl nitrite, as well as alcohol and marijuana, extensively. He indicated that his use of ethyl chloride (purchased in an aerosol canister, sprayed on a cloth, and inhaled) had increased as his use of amyl nitrite decreased, following published reports implicating amyl nitrite as either a cofactor in HIV infection or a direct immunosuppressant.

Given the evidence of both severe toxic effects and withdrawal reactions, as described in the aforementioned case reports, ethyl chloride abuse may be a complicating factor in differential diagnosis in individual cases. It may be useful to include questions regarding ethyl chloride abuse when interviewing individuals who have access to the agent through employment (ethyl chloride in spray form is used for treating musculotendinous pathology by physical therapists, sports trainers, etc.) (4) and those who have previously abused amyl nitrite.

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Injunction to Cover Cost of Clozapine

SIR: We are writing to call the attention of *Journal* readers to a temporary injunction ordered by U.S. District Judge Earl O'Connor to the State of Kansas to cover the cost of clozapine for a patient of ours who has treatment-resistent schizophrenia. Judge O'Connor found as a matter of law that the patient would suffer irreparable injury unless the injunction was issued, that her injury would outweigh whatever damage the injunction would cause the defendant (the secretary of the Kansas Department of Social and Rehabilitation Services), and that the injunction would not be against the public interest. The judge concluded that the defendant's refusal to cover the cost of clozapine was an arbitrary reduction in the scope of prescription drug services to otherwise eligible individuals solely on the basis of their illness or condition. The judge ordered the Department of Social and Rehabilitation Services to provide clozapine to the patient and, in addition, ordered the department to include clozapine in its formulary of drugs covered by the Kansas Medicaid program. While this case was not filed as a class action suit, our attorney informs us that it will have the same effect as that of a successful class action.

At this point the Kansas Department of Social and Rehabilitation Services is investigating how to implement this program in Kansas. It is possible that it will appeal this decision to the Tenth Circuit Court of Appeals. However, it does not appear likely that this will be its course of action. In the past the department has negotiated a settlement of a case once an injunction has been granted. This is the first case that we are aware of that mandates Medicaid payments for the drug clozapine by a state Medicaid program. The official at Care Mark who is responsible for the administration of the clozapine program for Kansas informs us that currently there are 49 patients in the program in the state (personal communication, Care Mark Co., September 1990). The $9,000 annual cost of clozapine therapy poses a barrier to wider use of the treatment, but it is important for psychiatrists to be aware of these legal issues so that they can be knowledgeable advocates for the best care available for their patients.

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Psychological Damage of Combat

SIR: This letter is in regard to what I believe is the presumption behind our thinking and research into posttraumatic stress disorder (PTSD) arising from military combat. The presumption is that a man should be able to fight in a combat zone and not experience some type of biopsychosocial consequence or injury because of it, or that if he does, he had some fundamental abnormality before he entered combat or after he left it. This presumption basically implies that combat between people is sufficiently normative to be undamaging—or that it should be undamaging.

I would like to suggest that this is a consequence of the *Zeitgeist* of our times, something that is in the background of our culture or the world's culture. Our current milieu says that a part of being male is to fight in a war or to be capable of it. And yet I find it hard to believe that any human being is made for trauma, is made to be traumatized, or comes through it unscathed. I find it hard to believe that men were made for wars. Perhaps the greatest thing that will come from PTSD research is that it will help us to rephrase our basic assumptions and, finally, to decide that what is truly normative for the male is to be a son, a lover, a father, and a grandfather, and not a soldier. Perhaps being exposed to combat is an equivalent of nuclear winter—that is, the effect on the societies engaged in warfare is so damaging to both sides that there are no winners, only damage to and ultimately the destruction of the human members.

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Ingestion of Sharp Foreign Objects

SIR: Many varieties of self-injurious behavior have been described in the psychiatric literature. In reports of bizarre acts such as autocastration or self-enucleation, the victims are usually psychotic and their acts are motivated by delusional ideas and/or hallucinations (1, 2). The more common phenomenon of repeated superficial slashing of body parts, usually the wrists, is often associated with borderline personality disorder (3). The purposeful ingestion of foreign objects has rarely been discussed in the psychiatric literature. Most reports of ingestion of foreign bodies have been about prisoners; less attention has been paid to ingestion of sharp objects by nonprison populations (4).

We examined the cases of six nonprisoners who were admitted to an urban public hospital's medical and surgical wards after deliberate ingestion of sharp objects outside of the hospital. They were seen by the psychiatric consultation service during hospitalization. We report on the characteristics of these patients and their reasons for ingesting these objects.

The six patients ranged in age from 20 to 53 years, with a mean age of 32 years. Five of the six patients were male. Half of the patients were intoxicated at the time they ingested the foreign object; two had abused alcohol and one had abused cocaine. All of these intoxicated patients were subsequently diagnosed as having substance dependence; one of the alcohol-dependent patients was concomitantly diagnosed as having schizophrenia. The diagnoses of the three patients who had not been intoxicated at the time they ingested the objects were schizophrenia, mental retardation, and personality disorder. Five of the six patients had received previous psychiatric treatment, and four had had previous psychiatric hospitalizations. Four patients had histories of suicide attempts; one attempt involved the swallowing of a foreign body.

The reasons for object ingestion were as follows. Two patients had responded to command hallucinations, two had been attempting suicide, one had wanted to harm but not kill himself, and one had exhibited regressive behavior in the context of mental retardation. Of the two who had responded to command hallucinations, one was intoxicated and one was not intoxicated; the same was true of the two who had attempted suicide.

It makes intuitive sense that patients who swallow sharp foreign objects have serious psychopathology, possible suicidal ideation, and past psychiatric hospitalizations. The number of patients with substance dependence and intoxication at the time of the act is more notable. The threshold for committing the swallowing act may be lowered by intoxication; drugs and alcohol appear to be associated with self-injury (5). When a patient presents with a history of swallowing sharp foreign objects, consideration of a diagnosis of substance abuse (and treatment if substance abuse is present) seems paramount.

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Services for the Homeless Mentally Ill

SIR: Before offering a caveat to the Commentary "Will We Save the Homeless Mentally Ill?" by H. Richard Lamb, M.D. (1), I would like to deliver to him a public encomium for his forthright position on the measures needed to deliver services to this population. While some might view his advocacy as reactionary, it is a sad irony that it might better be conceived of as left-wing radicalism!

I caution against undue emphasis on the homelessness of the contemporary American chronically mentally ill. Before they were visible victims of neglect in our communities, they were invisible victims of neglect in our state hospitals (2, 3). The focus should be on the act of neglect, not on the locus of the act.

How different is it, really, whether the chronically mentally ill eat (on cue) overcooked, starchy lunches in hospital cafeterias or eat (ad lib) discards at a neighborhood dumpster; or whether they sleep on command on rubber mattresses in overcrowded hospital wards or sleep at their discretion on heating grates along dirty city streets; or whether they beg for cigarettes in smoke-filled institution lobbies, when allowed to by hospital staff, or panhandle for spare change along subway platforms, when permitted to by city police?

Dr. Lamb offered several remedies for the current collection of wrongs. His suggestions, such as well-functioning case management, comprehensive crisis intervention, and outpatient civil commitment should continue to be tried. They should, however, be simultaneously evaluated, refined, and reevaluated. Psychiatry has too long a history of doing *to* the chronically mentally ill in the name of doing *for* the chronically mentally ill and, in the process, doing some pretty awful things (4).

The chronically mentally ill have gone from the Publick Gaol to the Public Hospital and back again between 1770 and 1990. It is less where they are housed (or unhoused) than how they are treated that need concern us. The public good requires as much.

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Dr. Lamb Replies

SIR: I fully agree with Dr. Geller that an overriding concern of mental health professionals should be the neglect in all its forms of the chronically mentally ill. I have been writing about these various forms of neglect for many years (1–3). I also believe that we must explore and attack each form of mistreatment of this vulnerable group. In this regard, allowing chronically and severely mentally ill persons to live on the streets, with all the horrors entailed in such an existence, seems to me to be the epitome of neglect. And we must bear in mind that the great majority of these persons are unable, because of their illness, to take action to do something about their plight; thus, they depend on us to take action for them.

Most distressing to me is that this situation has been discussed and written about for a decade, and yet very little has been done about it. For instance, the recommendations of APA's Task Force on the Homeless Mentally Ill (4), had they been implemented, would probably have greatly reduced the prevalence of homelessness among people with major mental illness. Little has been done, however, to implement these recommendations since they were published in 1984.

Obviously, I am not recommending returning these persons to the conditions under which they lived in the back wards of the state hospitals of the past. I do believe, however, that we need to do something definitive—and soon. We want to have comprehensive and coordinated mental health systems that will engage the homeless mentally ill and help many of them voluntarily accept treatment and suitable living arrangements. But the homeless mentally ill cannot wait decades for these systems to be established. Moreover, many homeless mentally ill persons will not accept services, even with assertive outreach case management. In the meantime, if homeless persons with major mental illness are incompetent with regard to accepting treatment, present a danger to themselves or others, and/or are gravely disabled, I believe that outreach teams including psychiatrists should bring them to hospitals, against their will if need be.

If, after a relatively brief period of hospitalization, these persons can be placed voluntarily in suitable living situations with built-in ongoing treatment, then we need to have these resources available. I believe that although we should have high standards for treatment and supportive housing, we cannot in good conscience leave the homeless mentally ill on the streets while we wait for such resources to be developed.

In the short run we should settle for resources that are acceptable, if not ideal.

It is my belief that the time for endless and fruitless discussion is long past, and action is long overdue.

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Los Angeles, Calif.

Elderly Patients' Decisions About Care

SIR: The letter from Richard M. Berlin, M.D., regarding elderly patients who refuse to eat (1) highlights a clinical problem of increasing frequency. As a consultant to a psychogeriatric service, I am regularly asked to see inpatients who are refusing to accept food or fluids, but with a view to assessing their competence rather than diagnosing any underlying psychiatric disorder. The majority of these patients are in long-term care and are fully investigated. Diagnoses are well-established and treatments are usually optimal. The service has access to an expert swallowing and meal management team consisting of a psychiatrist, dietician, and speech-language pathologist who provide an anatomical and pathological diagnosis where relevant, complemented by esophageal videofluoroscopy.

The Province of Alberta in 1988 adopted a new mental health act that, in common with the majority of such legislation in North America, allows competent patients the right to refuse treatment. The medical profession is well aware of the current public and media focus on passive euthanasia, living wills, and physician-assisted suicide, yet the issues facing clinicians caring for individuals who are both medically debilitated and psychiatrically ill are even more medicolegally complex. The central issue is whether or not the individual has made a conscious decision to die based on a full understanding of his or her medical condition. Forced nasogastric tube feeding and intravenous hydration are inevitably major considerations in these cases, and the wishes of the patient, responsible relatives, and any legally appointed guardian have to be taken into account. A refusal to accept nourishment that is based on delusional thinking is rare in this age group and is relatively easily identified. It is more difficult, however, to separate clinical depression with suicidal ideation from what can be termed "philosophical terminal resignation." A strictly legalistic approach that would necessitate applications to review panels for involuntary treatment orders (as would occur if the patient were refusing psychotropic treatment) is ethically unsatisfactory besides taking too long. Relatives and guardians usually have well-thought-out opinions on these issues, but a conflict can arise when the psychiatrist feels that there is a treatable condition responsible for a temporary loss of competence but a relative refuses to sanction any intrusive measures.

The gradual aging of psychiatric inpatient populations, which parallels the trend in the community at large, will lead to an increase in this type of ethicolegal problem, a situation not covered by traditional mental health legislation. It may well be that some physically debilitated individuals are suffering needlessly prolonged deaths because their wish to decline further medical intervention is deemed invalid, since it was previously documented that they were incompetent to consent to treatment because of psychiatric illness. In order to negotiate these potentially complex medicolegal issues, clinicians working with chronically debilitated psychiatrically ill patients need to develop and standardize guidelines for assessing competence to refuse medical interventions that take into account the accepted ethical and moral values of their local community, the mental health laws of their particular state or province, and the expressed wishes of the patient or guardian.

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Dr. Berlin Replies

SIR: I appreciate Dr. Holden's thoughtful letter, which focuses on the issue of competency in elderly patients who are debilitated and refuse to eat. Consultation-liaison psychiatrists are often asked to evaluate elderly patients for competency (1). Most patients who are considered incompetent after psychiatric consultation are diagnosed as having an organic mental disorder, usually delirium or dementia (2). A number of excellent communications provide guidelines for assessing competency (3), emphasizing legal principles, the importance of conducting a thorough clinical examination, risk-benefit issues, communication with the referring physician and nursing staff, and the requirements of the consultant's written note. In our hospital, we have developed a family-oriented approach that emphasizes active, direct family involvement in every competency evaluation (4).

While a majority of Dr. Holden's patients have been thoroughly examined, a recent report (5) suggests that psychiatrists assessing patients' competence may overlook the need for psychiatric interventions, especially supportive psychotherapy and family involvement. I believe, as Dr. Holden suggests, that consultation-liaison psychiatrists should aid in developing standards to assess competency. In addition, when asked to evaluate patients for competency, we must not overlook our role as clinicians skilled in providing psychiatric treatment for patients and their families.

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Anxiety Disorders in Familial Parkinsonism

SIR: We congratulate Murray B. Stein, M.D., F.R.C.P.(C), and associates on their article on anxiety disorders in Parkinson's disease (1). We previously presented results of a similar study of 28 patients with familial parkinsonism. We summarized some of those findings in a brief published abstract (2), and we report others here.

We found lifetime prevalences for the following *DSM-III* anxiety disorders: generalized anxiety disorder, 5.3%; panic disorder, 7.9%; social phobia, 5.3%; agoraphobia, 15.8%; simple phobia, 34.2%; and obsessive-compulsive disorder, 13.2%. Thus, the prevalence of generalized anxiety disorder was similar to that in Dr. Stein and associates' study, while our study found less panic disorder and social phobia and more obsessive-compulsive disorder. We found a similar number of patients with embarrassment about their parkinsonism (five in our study). We also found that the psychiatric disorders preceded and followed, respectively, the onset of parkinsonism in the 28 subjects as follows: panic disorder, three and one; social phobia, 12 and zero; agoraphobia, six and four; simple phobia, 13 and two; and obsessive-compulsive disorder, five and two. Thus, in our sample only agoraphobia and obsessive-compulsive disorder seemed to begin after the onset of familial parkinsonism.

We also found 14 cases of atypical anxiety disorder (panic-attack-like phenomena) that did not quite meet the criteria for panic disorder. Eight preceded and six followed the onset of parkinsonism. Several true cases of panic disorder underwent a modification of their course after the onset of the "freezing" phenomenon of parkinsonism. We found no relation to the "on-off" phenomenon, in accord with the findings of Dr. Stein and colleagues.

Differences between the results of our study and those of Dr. Stein and associates might be accounted for by more widespread neuropathology in familial parkinsonism than in idiopathic Parkinson's disease. It is possible that greater involvement of the raphe nuclei, nigroventro tegmentum, and locus ceruleus account for more obsessive-compulsive disorder, agoraphobia, and atypical anxiety in patients with familial parkinsonism, although this remains to be proven.

Dr. Stein and colleagues cited improvement of anxiety disorders with benzodiazepines. We would add the caution that benzodiazepines can, at times, worsen parkinsonian symptoms.

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Addition of Fluoxetine to Treatment of Schizophrenic Patients

SIR: Donald C. Goff, M.D., and associates reported on a pilot study in which the selective serotonin (5-HT) reuptake blocker fluoxetine was added to the neuroleptic treatment of chronic symptomatic schizophrenic and schizoaffective patients (1). Nine of 14 treatment-resistant schizophrenic patients completed a 6-week open trial of 20 mg of fluoxetine added to their neuroleptics. Five patients dropped out because of side effects. The nine completers showed statistically significant decreases not only in depression as measured by the Hamilton Rating Scale for Depression but also in positive and negative symptoms of schizophrenia as measured by the total Brief Psychiatric Rating Scale (BPRS), the Scale for the Assessment of Negative Symptoms, and the Global Assessment Scale. Decreases were noted on the BPRS items for suspiciousness, hallucinatory behavior, conceptual disorganization, and unusual thought content. Four of the nine patients were rated by their primary clinicians at week 6 as moderately or much improved. The authors contrasted their findings to those of a study in which imipramine was added to neuroleptics in schizophrenic patients with major or minor depression (2). In that study, depressive symptoms improved, but positive and negative symptoms of schizophrenia did not improve.

Dr. Goff and associates discussed possible mechanisms for improvement in schizophrenic symptoms with fluoxetine. They suggested that in some neuroleptic-resistant schizophrenic patients, fluoxetine may correct a presumed abnormality in 5-HT regulation. Also, fluoxetine may act indirectly in responders by regulating dopaminergic activity; i.e., serotonergic pathways exhibit complex interactions with dopaminergic systems, including inhibitory regulation of activity of forebrain dopamine-containing areas (3). The authors also noted the complexity of multiple types of 5-HT receptors and difficulty in predicting the effects an agonist or antagonist might produce. Hypothetical subtypes of chronic neuroleptic-resistant schizophrenia have been proposed to reconcile the confusing literature on serotonin and schizophrenia (4).

In clinical open trials, we added fluoxetine, 20 mg/day, to the neuroleptic and other medications taken by 21 cooperative, chronic, treatment-resistant schizophrenic or schizoaffective male outpatients diagnosed according to *DSM-III-R*. These were patients we had followed regularly over many years who returned for reevaluations at monthly intervals. Most had mixtures of positive and negative symptoms, and some appeared depressed and anergic despite adjunctive medications that included lithium and tricyclics. We found mild to moderate improvements in energy, anxiety, and mood in 11 of the 21 patients after fluoxetine was added. Only three of these patients reported hearing voices less frequently, two mildly and one markedly. In two responders the dose of neuroleptic was reduced. Of the 10 other patients, three reported considerably more paranoia and hearing of voices, and one of these patients showed increased tardive dyskinesia; fluoxetine was rapidly discontinued. Three others quickly discontinued fluoxetine because of headaches, gastrointestinal cramps, or vomiting. The other four patients noted no improvement in mood or other symptoms after a month with added fluoxetine, so it was discontinued.

In view of these results, we suggest guarded optimism in the use of fluoxetine in treatment-resistant schizophrenic or schizoaffective patients, as we found that even some patients whose illness had depressive features became considerably worse. Nevertheless, the positive responses, mostly in mood and energy, in over half the patients were significant. We agree with Dr. Goff and associates that controlled double-blind studies are indicated.

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Dr. Goff and Associates Reply

SIR: We were interested to learn of the experience of Drs. Bacher and Ruskin suggesting that addition of fluoxetine to neuroleptics may improve energy and mood in some schizophrenic patients. This finding is consistent with the hypothesis which we undertook to test in our open pilot study—that fluoxetine would improve negative symptoms of schizophrenia. In addition to improvements in mood and negative symptoms, we were surprised to find impressive improvement in positive symptoms in four of the nine patients who completed our 6-week trial; however, we note that Drs. Bacher and Ruskin observed such an effect in only one of 18 completers. We are currently conducting a double-blind trial to clarify this issue.

The worsening of psychosis and of tardive dyskinesia reported by Drs. Bacher and Ruskin is obviously of serious concern. We have not observed either of these effects in the 30 patients whom we have studied in open trials, but other clinicians have described to us cases in which agitation worsened after addition of fluoxetine to a neuroleptic. In a separate trial, we observed a minimal effect of fluoxetine on extrapyramidal symptoms despite a modest increase in haloperidol blood levels (unpublished data). Lipinski et al. (1) described akathisia associated with fluoxetine administered as a single agent, and others have observed worsening of extrapyramidal symptoms after addition of fluoxetine to neuroleptics (2).

We agree with Drs. Bacher and Ruskin that combined treatment with fluoxetine and neuroleptics holds clinical and theoretical interest; however, double-blind trials are needed to establish clinical benefit as well as to assess the risk of adverse effects. As Drs. Bacher and Ruskin point out, it may be a subgroup of treatment-resistant psychotic patients who benefit from this combination.

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Organic Mental Disorders Caused by HIV

SIR: In a review of organic mental disorders caused by HIV, Samuel W. Perry, M.D. (1) presented a summary of 20 studies on early neuropsychological impairment in adults at risk for AIDS. Results of these studies were mixed; 10 groups reported neuropsychological impairment in patients with stage II or stage III HIV infection, whereas 10 other groups found no impairment. It is important to note that intravenous drug abusers were represented in only five of these studies—three had "mixed" subjects and two had exclusively intravenous drug abusers.

In a recently completed study of drug abusers who participated in an outpatient treatment research program (unpublished 1990 paper), my colleagues and I matched 22 HIV-antibody-positive (Centers for Disease Control stage II HIV infection) cocaine addicts to 22 HIV-antibody-negative cocaine addicts. We compared retention in treatment and mood states over the 12-week treatment course. At intake, when we and the subjects were blind to their HIV antibody status, we evaluated subjects using the Cognitive Capacity Screening Examination (2), the SCL-90-R (3), and the Shipley Institute of Living Scale (4). We found no significant differences between the groups in sociodemographics, psychiatric symptom scores, or intellectual functioning and cognitive impairment. We followed subjects' mood after they were informed of their HIV antibody status and over the 12-week treatment study and found no significant differences between groups in suicidal ideation or mood states except for "anger/hostility." There was a statistical trend for more seropositive subjects to complete treatment.

Although our study would fall in Dr. Perry's category of studies with the least extensive neuropsychiatric batteries, it does offer data regarding the cognitive and intellectual functioning of HIV-infected drug addicts. More important, results of our study suggest that informing drug abusers in treatment about their seropositive HIV status was not associated with a lower treatment-retention rate or adverse psychological reactions when counseling regarding HIV issues was integrated with drug abuse treatment.

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Dr. Perry Replies

SIR: Few systematic studies of drug users have examined psychological responses to HIV testing (1) or compared neuropsychological impairment in those who are and are not infected (2). Dr. Weddington and his colleagues are therefore to be commended for their efforts; however, the brief summary of their study does not help answer many relevant questions.

Regarding the emotional impact of being notified about serological status, one wonders how the seropositive cocaine addicts became infected; whether they were equivalent to the seronegative addicts at entry in terms of psychiatric diagnosis, psychological status, current and past drug use, and HIV risk behaviors; whether the sample size was large enough at follow-up to detect psychological differences; whether the SCL-90-R alone is sensitive and specific to AIDS-related distress; whether relapse into drug taking was associated with notification; and whether the subjects were followed long enough for the findings to be clinically meaningful, considering the length of time the seropositive subjects will live with the knowledge of having a fatal illness.

Regarding the absence of differences in neuropsychological impairment between seropositive and seronegative patients, the Cognitive Capacity Screening Examination is not sensitive to subtle cortical, and especially subcortical, deficits among CDC stage II patients (2).

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Lithium Treatment of Cocaine Addiction

SIR: In their article on lithium treatment for cocaine abusers (1), Edward V. Nunes, M.D., and associates reported little if any benefit from lithium, and this has been my experience. Theoretically, lithium should help moderate the mood swings so characteristic of cocaine addiction and recovery. Cocaine abuse has long been associated with affective disorders, especially depression, cyclothymia, and bipolar disorders (2). It is not clear, however, whether these are caused by or are the result of cocaine abuse. Recently, it has become evident that cocaine patients become addicted as much by pursuing euphoria as by self-medicating for dysphoria. In cyclothymic addicts, cocaine is used more during the hypomanic phase than during depression (3, 4).

An investigation of 292 primary cocaine addicts, treated at a hospital, showed that 22% had abused cocaine while seeking relief from preaddictive dysphoria or depression, and 13% had become addicted while seeking to enhance the euphoria that they had always enjoyed because of a hypomanic personality trait (5). The majority (63%) of these 292 patients had always thought of themselves as normal, with no significant emotional or adjustment problems before their addiction.

If patients are in a dysphoria phase of recovery, lithium may make them feel worse by further "slowing them down." If they are in an "up" mood of excitement over feeling good about themselves and their recovering, they may not want these feelings blunted by lithium. It is conceivable that lithium may even be contraindicated in some patients being treated for cocaine addiction. Several such patients have told me that they stopped taking lithium because it had dulled and taken the edge off the zest, enthusiasm, and feeling of joy about recovering.

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Dr. Nunes Replies

SIR: We are very interested to learn that Dr. Lemere shares our disappointing experience with lithium in bipolar spectrum cocaine abusers. We would only caution that a hypomanic or cyclothymic presentation should alert the clinician to inquire carefully about past history or family history of full-blown mania. True bipolar I disorder, although relatively rare in cocaine abusers (1–3), would still be a strong indication for lithium therapy as an adjunct to drug rehabilitation treatment.

Dr. Lemere's finding that a substantial minority of his cocaine-abusing patients suffered some form of mood disturbance further highlights the possible importance of affective disorder in cocaine abuse. However, the differential diagnosis of these mood disturbances remains broad, and the question of the relation between substance abuse and comorbid syndromes is complex (4, 5).

The hypomanic pattern could represent cocaine-induced mood swings—i.e., organic affective disorder—or one of several independent disorders, including borderline or histrionic character disorder with prominent mood swings, atypical depression with marked mood reactivity (elevated mood in response to positive events), cyclothymic disorder, or bipolar II disorder. The substantial problem posed for clinical practice and research is to distinguish these diagnostic alternatives in cocaine abusers and delineate the treatment implications.

The dysphorias observed by Dr. Lemere were "preaddictive," presumably meaning that their onset was reported to have occurred before the onset of substance abuse. This is important information and suggests an independent disorder rather than the organic alternative, but it is by no means confirmatory. The historical recall may not have been accurate. Further, the fact that a mood disturbance predated substance abuse does not prove it was the same as the current mood disturbance. A variety of clinical data need to be considered, including mood during past periods of abstinence or recovery, mood after a current course of detoxification, relation of mood to episodes of relapse, family history, and, finally, results of therapeutic trials.

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Role of Cholecystokinin in Irritable Bowel Syndrome

SIR: Edward A. Walker, M.D., and associates (1) reviewed the evidence for psychiatric symptoms in patients with irritable bowel syndrome and offered a pathophysiological model for this syndrome. They postulated that some brain-gut peptides might play a neurobiological role in the syndrome and that the CNS link between psychiatric disorders and irritable bowel syndrome might be the locus ceruleus. As they briefly mentioned, cholecystokinin may be one of the peptides that could account for the psychiatric symptoms reported by patients with irritable bowel syndrome.

We have reported that cholecystokinin tetrapeptide induces panic attacks at a higher rate in patients with panic disorder than in healthy volunteers (2). Patients reported that the panic attacks induced with cholecystokinin tetrapeptide were very similar or identical to their natural panic attacks (3). Cholecystokinin might also account for the gastrointestinal symptoms that often accompany panic disorder. At least 60% of a total of 45 patients in whom panic has been induced so far have reported nausea or gastrointestinal discomfort during the induction. These patients have also experienced these same symptoms during spontaneous panic attacks.

The neuroanatomical link proposed by Dr. Walker and associates is also consistent with an involvement of cholecystokinin. This peptide is present in the neocortex, in the limbic system, in hindbrain structures such as the periaqueductal gray, the nucleus raphis dorsalis, and the area postrema, and in the nucleus tractus solitarii (4), which is postulated by these authors to serve as a relay to the locus ceruleus.

Benzodiazepines have shown efficacy in anxiety disorders and, as mentioned by the authors, possibly in irritable bowel syndrome. Benzodiazepine receptor agonists antagonize cholecystokinin-induced excitation of limbic neurons (5) and can also antagonize the gastrointestinal effects of cholecystokinin (6).

Provocation studies with cholecystokinin in patients with irritable bowel syndrome, similar to the ones conducted in patients with anxiety disorders, might elucidate the role of this peptide in the gastrointestinal and psychiatric symptoms of the syndrome. We suggest the use of the tetrapeptide form of cholecystokinin rather than larger forms, which have been used in gastrointestinal studies but which have not been shown to induce anxiety symptoms. Therapeutic trials with cholecystokinin antagonists might also help elucidate the role of cholecystokinin in both anxiety disorders and irritable bowel syndrome.

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SIR: In the helpful review by Dr. Walker and associates, we were concerned about one thing: the implication that psychological factors are useful in the diagnosis of irritable bowel syndrome. We agree that psychological factors are associated with the syndrome but disagree that they assist the clinician in distinguishing it from the organic diseases that may present similarly.

We recently studied this question prospectively in 97 new patients presenting with abdominal pain, altered bowel habits, or both (1). Our report was published after the paper by Dr. Walker and his colleagues was accepted, and therefore it would not have been available to them. All patients underwent full evaluation by gastroenterologists in an outpatient setting and were followed for 9 months. We predicted that six psychosocial measures representing the psychological changes associated with irritable bowel syndrome (anxiety, depression, stress, lack of social support, somatization, and abnormal illness behavior) would distinguish the patients with this syndrome from those with organic diseases. Irritable bowel syndrome was defined as the absence, at the conclusion of the 9-month study, of an organic disease that could explain the patient's complaints at the time he or she entered the study; the determination was made by independent raters. Approximately two-thirds of the study group had irritable bowel syndrome, and one-third had various organic diseases. None of the psychosocial predictors distinguished the patients with irritable bowel syndrome from those with organic diseases; the power of the statistics was satisfactory. Further analysis revealed that the patients with organic diseases as well as those with irritable bowel syndrome had significantly more psychosocial abnormality than is reported for normal subjects. The study thus corroborated the strong association of psychological factors in patients with irritable bowel syndrome, but in demonstrating similarly high scores for patients with organic diseases, it showed that psychological factors are of little diagnostic value. The study highlights the importance of psychosocial factors as determinants of health-care seeking, whether this is due to irritable bowel syndrome or organic disease. Moreover, it demonstrates what the biopsychosocial model (2) tells us—that psychosocial factors are present in most medical patients, whether they have organic or nonorganic disease. The findings of our study should not raise questions about the fundamental importance of psychosocial factors in treatment, understanding the patient, and establishing a therapeutic relationship.

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Dr. Walker and Associates Reply

SIR: We appreciate the observations of Dr. Bradwejn and associates on the effect of cholecystokinin on the production of gastrointestinal symptoms during panic attacks. Their observations were unavailable to us at the time of our review; however, the findings offer an exciting research opportunity in the provocative testing of the enteric nervous system. Despite recent advances in establishing diagnostic criteria, irritable bowel syndrome remains a diagnosis of exclusion. This increases the likelihood that this syndrome could be a heterogeneous group of disorders, and provocative tests such as this may assist in the proper subdivision of irritable bowel syndrome into more specifically defined motility disorders. The observations of Dr. Bradwejn and associates illuminate what may become a fascinating future direction for research on irritable bowel syndrome.

We agree with Drs. Smith and Greenbaum that psychological factors are not useful in discriminating irritable bowel syndrome from other gastrointestinal disease. After a careful review of our article, we were unable to find any statements that appeared to imply that they would be helpful in differential diagnosis. We also cited a number of studies that agree with the observation by Drs. Smith and Greenbaum that health-care-seeking behavior is an important determinant in the development and maintenance of irritable bowel syndrome. The work of Drossman and associates (1, 2) has shown that patients with irritable bowel syndrome are more likely to complain of nongastrointestinal symptoms and have higher rates of physician utilization than patients without irritable bowel syndrome. These patients also have a higher proportion of abnormal personality patterns, more illness behavior, less coping capability, and more experience of symptoms causing disability than people who have these gastroenterologic symptoms but do not visit physicians. Thus, although the psychological factors may not assist in diagnosis, they appear to play an important role in the treatment of patients with irritable bowel syndrome.

We recently completed a study comparing 28 patients with irritable bowel syndrome and 19 patients with inflammatory bowel disease (3). Like Drs. Smith and Greenbaum, we found no significant differences between the groups on several self-report measures, such as the Beck Depression Inventory, the Spielberger State-Trait Anxiety Scale, the Modified Somatic Perception Scale, and the SCL-90. However, structured psychiatric interviews with the Diagnostic Interview Schedule showed highly significant differences in lifetime history of major depression, panic disorder, and somatization disorder, as well as a number of medically unexplained somatic symptoms involving many organ systems. This suggests that although patients with irritable bowel syndrome and those with other organic diseases may be distressed at the time symptoms appear, the patients with irritable bowel syndrome may possess an additional chronic disability that is periodically expressed through psychiatric disorder. Thus, information about the longitudinal course of illness and coping may be important, while cross-sectional self-report measures alone may be inadequate to distinguish between the two kinds of disorders.

Regardless of these differences, Drs. Smith and Greenbaum have reminded us of the value of biopsychosocial evaluation in all medical diseases and the importance of comprehensive treatment planning.

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Managed Care and Psychiatry

SIR: As Lloyd I. Sederer, M.D., and R. Lawrence St. Clair, M.D., noted in their very interesting article (1), it is beyond doubt that the exploding costs of the fee-for-service, unregulated health system in the United States demand new ideas and decisions. However, it is questionable whether managed care can provide a functioning alternative.

Organizations that, for a flat fee, provide through their own hospitals and doctors (or outsiders with whom they contract) all the care a customer needs may probably be the newest trend in the United States. In Europe they have, however, a not-so-glorious tradition. For example, 1) in Great Britain the National Health Service has produced since 1948 months-long waiting lists and runaway costs; 2) in Greece the Institution for Social Security, compulsorily subscribed to by most employees, ran a \$1.62 billion deficit in 1989. The folk wisdom that doctors' motivation has a materialistic basis also leads patients to prefer the additional financial burden of a fee-for-service treatment in the free market to a compulsorily prepaid but poor-quality one.

Even in the United States, managed care has not proved the simple route to lower costs that its advocates hoped for. Financial experts estimate (2) that after an initial saving, the costs of these schemes have risen as fast as those of their unmanaged rivals. What, really, is the Massachusetts experience with costs?

Nevertheless, managed care in psychiatry poses quite serious ethical questions. As Drs. Sederer and St. Clair rightfully stated, "Physicians have found that their fiduciary relationship . . . with patients has been increasingly eclipsed by a contractual relationship with corporations." Furthermore, what about the primary need of the mentally ill to freely choose a therapist in whom they can put trust and confidence? In the case of a dysfunctioning doctor-patient relationship, is a change of therapist an inflationary act? Can the bureaucratic machinery of a "second opinion service" realize and appraise the quality of the therapeutic encounter? Is not the customer the ultimate judge?

Freedom of choice is not contradictory to efficiency. In West Germany the almost ubiquitous compulsory health insurance does not restrict the right to free choice of a doctor. Annual reimbursements by the private insurers to cost-conscious patients provide them with financial incentives to refrain from overutilization of services.

We think that in the search for financially and morally acceptable alternatives in health care costs, American medicine should not neglect the experience of its counterparts in the Old World.

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Drs. Sederer and St. Clair Reply

SIR: We thank the Drs. Vartzopoulos for their thoughtful comments. The New World certainly has no monopoly on wisdom regarding health care. We will need to look to Canada, to the Old World, and to Asia for ideas and models on how to integrate access, quality, choice, and value.

Our article endeavored to identify the social forces compelling the managed care movement, to acknowledge its contributions, and to emphasize its potential problems. Among the "solutions" to those problems are a variety of regulatory and consultation (second opinion) services that we also outlined, not without concern for the additional problems that derive from regulation. Our aim was not to prescribe these solutions but to offer a set of options that clinicians, patients, and families might use in defending themselves against those managed care practices that are unfair and frankly deleterious to the health and welfare of patients.

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Nutritional Treatment of Tardive Dyskinesia

SIR: The confirmation by Ahmed M. Elkashef, M.B.B.Ch., and associates (1) of Lohr et al.'s demonstration of vitamin E's efficacy in reducing tardive dyskinesia (2) was very welcome. Any time a treatment advance can be made by using nutrients only, it should be very good news and should be pounced upon by psychiatrists and other physicians, as the benefits are not limited to the target symptoms only, and deleterious effects can be eliminated by keeping plasma levels within the normal range.

So often, though, for some reason, nutritional research reports are not taken advantage of and applied in everyday practice and mainstream thinking about psychiatry. For example, Dr. Elkashef and associates used a 1982 book as a reference for their contention that, until the work immediately prior to their own on α-tocopherol, there was no useful treatment for tardive dyskinesia. However, numerous research reports throughout the 1960s and 1970s culminated in several investigators' 1975–1979 discoveries of the effects of lecithin in reducing tardive dyskinesia, well summarized in another 1982 book (3). Quite separately, others found diminution of tardive dyskinesia with use of vitamin B_6 (4) and manganese and (to a lesser extent) niacin (5). I cannot reference all the lecithin research because I am limited in the number of references I can use in a letter, but the researchers included K.L. Davis, P.A. Berger, L.E. Hollister, J.M. Davis, A. Barbeau, A.J. Gelenberg, J.C. Doller-Wojcik, the Brancheys, I.V. Jackson, and many others.

The beneficial effect of paying attention to *all* these nutritional parameters, in addition to the many others that are focused on in a nutritionally oriented practice, is that there is apparently little or no tardive dyskinesia in hospitals that use orthomolecular/megavitamin therapies (4), and I can attest to the absence of this dreaded chronic side effect of neuroleptics in my own nutritionally oriented psychiatric practice. Even if many of the claims of the orthomolecular/megavitamin psychiatrists and physicians have, quite correctly, been discarded, there are many that deserve more attention. This one seems to me to be prime among these claims.

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Mechanism for Effect of Benztropine on Bed-Wetting

SIR: In response to the letter from Jerome F. Costa, M.D., and associates on controlling bed-wetting with benztropine (1), it seems that several pertinent clinical and biochemical facts need to be clarified. This report of benztropine's efficacy in controlling urinary incontinence actually was further support of a previously proposed hypothesis regarding urinary incontinence secondary to neuroleptics. Initially, it was clinically noted that urinary incontinence is a central parkinsonian side effect of neuroleptics which has been reported systematically with various classes of neuroleptic agents (2). Furthermore, it was noted that the antienuretic effect of tricyclics is clearly not secondary to their intrinsic anticholinergic, α-adrenergic, antidepressant, or sleep-stage effects (3). Especially regarding benztropine's anticholinergic activity, it is known that pure anticholinergic agents are not effective in treating enuresis in children (4).

A proposed alternative hypothesis was that antienuretic agents may be effective because they alter, in particular, balances of dopamine and norepinephrine (3). In partial support of this position is the fact that amantadine hydrochloride, a dopamine agonist and dopamine-releasing agent, effectively reduced enuresis in children by 41% (5).

It should be noted that benztropine, in addition to being a potent anticholinergic agent, is one of the most potent agents in blocking dopamine reuptake (6). It therefore seems a likely alternative hypothesis that the antienuretic benefit of benztropine is due to its effect on this neurotransmitter system. Clearly, well-designed studies of the efficacy of a varied spectrum of dopamine uptake blockers in enuresis are important in order to further understand the pathophysiology of this illness and to clarify more specifically central neurological control over peripheral activities.

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Use of "Syntonic" to Describe a Factor Common to Several Disorders

SIR: James I. Hudson, M.D., and Harrison G. Pope, Jr., M.D., in their important paper on affective spectrum disorder (1), identified a group of psychiatric disorders whose kinship is demonstrated by a similarity of response to antidepressant medication. In referring to the factor that these disorders apparently have in common, they used the scientifically correct term "common physiologic abnormality."

Eugen Bleuler's term "syntonic" (2) would be an appropriate descriptive term for this hypothesized common physiologic abnormality. Syntonic, which was originally a musical term, means being in harmony, as when one musical instrument is in tune with another. Bleuler apparently saw this as a companion and contrasting term to the other word he introduced, namely, "schizophrenia." He was considering the observation that, in certain cases of advanced schizophrenia, there is a discrepancy between the content of thought and the mood, whereas in depression the content of thought is in harmony with the mood. Although Bleuler was considering only major depressions in this regard, the term "syntonic" might also apply to the other disorders identified by Drs. Hudson and Pope.

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Issues Related to Cults and Zealous Self-Help Movements

SIR: The article "Cults and Zealous Self-Help Movements: A Psychiatric Perspective" by Marc Galanter, M.D. (1) covered the subject well but, in my opinion, lacked depth in certain areas. The first issue is that of dual diagnoses—and which is the primary diagnosis. Who decides? Alcoholics Anonymous (AA) for the alcoholic, the physician (alcoholism has been declared a disease), or the alcohol counselor? Second, does membership in a cult suggest dependency, zealousness, and addiction or a disease? Who decides? Third, how much does the professional person "turn over" to the amateur psychiatrist, the amateur psychologist, the amateur theologian, or the amateur group leader? Does training matter—or only (or mainly) the individual recovering from alcoholism or the person needing religion? Fourth, does the concept of disease have any limits? Does addiction? Is there a disease of religion?

I believe these troubling areas require adequate attention.

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SIR: In his otherwise uniquely interesting and informative article on cults and self-help movements, Dr. Galanter was overly parsimonious in covering the literature that has relevance to group psychology. To begin with, his definition of group cohesiveness, coined in 1960, has since then become the subject of much criticism in social psychology. In fact, Kaul and Bednar (1) concluded that "cohesion and cohesiveness have been a spectacular embarrassment in group theory and research. Over 30 years of effort has not enabled us to achieve an acceptable definition of terms."

I found it also especially regrettable that the extensive literature on psychoanalytic group psychology, which deals with the covert, emotional factors underlying such phenomena as cohesiveness, was not mentioned at all. There is, for example, a directly applicable recent contribution by Balter on charismatic groups (2). This is in addition to the earlier writings of such people as Freud, Redl, and Bion, which have been reviewed by Kernberg (3).

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Dr. Galanter Replies

SIR: Dr. Scott raises additional issues regarding the psychology of cults and zealous self-help movements, and these merit attention. Certain of these groups, AA included, clearly have a constructive role to play in relation to mental health needs, and because of this, it is important to delineate the optimal relationship between the nonprofessional (such as the AA member or the alcohol counselor) and the professional (such as the psychiatrist). Little research has been done in this regard and, certainly, more systematic attention needs to be paid to the issue.

It is both challenging and difficult to differentiate between individual psychopathology and socially grounded deviancy generated in zealous groups. In general, deviancy—whether behavioral, perceptual, or cognitive—should be assessed in relation to its compatibility with the norms of the group. If it is not compatible with the norms of the group, then the individual may well be evidencing primary psychopathology rather than deviancy promoted by the group. Certain classic signs of mental illness, such as thought disorder, may also be revealing and may well persist after the individual leaves the group. Deviancy predating the encounter with the group suggests preexisting pathology.

Is there a "disease of religion"? Certainly, religious activities can be directed at diverse ends and can influence members toward either positive or negative ends. A judgment on these matters must often be left to history, as objectivity is a rare commodity in this arena and may be hard to attain during the historical period in which events take place.

Dr. Scheidlinger is apt in pointing out the difficulty of defining certain constructs from social psychology such as group cohesiveness. The difficulty in making these terms operational in a research study can be compared to problems posed by their counterparts—for instance, the various affective states—in studies of individual psychology. These aspects of individual motivation and subjective state are not easy to define, just like group concepts such as cohesiveness and social support. Nevertheless, all are clearly important to understanding behavior.

The utility of the term "cohesiveness" cannot be dismissed and, indeed, much attention has been paid to its clinical application in therapy groups by authors such as Kellerman (1) and Yalom (2). In relation to cults as well, I have attempted elsewhere to examine the literature on group cohesiveness at greater length (3). I based my original choice of instruments to measure this phenomenon on the social psychological studies of Schutz, who has provided a practical instrument for this purpose, one with face validity as well as empirical validation (4).

Although Dr. Scheidlinger questions the utility of the concept of cohesiveness, he also suggests that the psychoanalytic literature on this topic should be mentioned. I have done this elsewhere (3) but do appreciate the value of the references that he has noted.

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Literature on Sun Gazing

SIR: A letter to the Editor from Peter S. Kamp, M.D., and associates (1) presented two cases of sun gazing by psychiatric patients and stated that a literature review revealed only one reference on the topic. In fact, Anaclerio and Wicker (2) reported an epidemic at a federal mental hospital in which 27 chronic schizophrenic patients injured their eyes by gazing at the sun. Deliberate sun gazing, with an intent to cause blindness, by a "neurotic" 17-year-old girl has also been reported (3). The topic is discussed and additional cases are presented in my book (4).

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Dr. Kamp and Dr. Rosse Reply

SIR: One of the reasons we decided to publish the cases of sun gazing by psychotic patients was our surprise that we could not easily find much literature on the subject with a computerized literature search. Although the behavior appears to be rare, it seemed worthy of attention because of its potentially serious consequences. Interestingly, one of us (P.K.) came across another case after our original submission; his ability to discover the sun gazing of this patient was due to his being sensitized to the existence of such behavior. We appreciate Dr. Favazza's pointing out earlier journal articles on the subject and regret our not finding his 1987 book with material on sun gazing in our computerized "review of the literature." Our computerized literature search included journals only. We did not do a CATLINE search, which might have captured the relevant book, although this would have been unlikely because of the limited number of subject headings or key words associated with a CATLINE entry.

Perhaps relevant to this discussion is Bareta et al.'s study (1) comparing manual and MEDLARS computerized literature searches of journals; manual searches appeared more successful. The *American Journal of Ophthalmology*, the source of the 1966 and 1970 articles on self-induced solar retinopathy noted by Dr. Favazza, would have been a reasonable journal to search manually in an effort to do a complete literature review. Books on self-mutilation would also have been worth investigating.

Dr. Favazza's letter seems to set the record straight on the status of the literature on sun gazing, and perhaps it is also a comment on the limitations of computerized literature searches. We hope that our letter and Dr. Favazza's discussion of the issue in his letter and book serve to further alert the psychiatric community to the potentially dangerous behavior of sun gazing.

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Reprints of letters to the Editor are not available.

THE AMERICAN JOURNAL OF PSYCHIATRY

Special Articles

Genetics and Psychiatry: An Unheralded Window on the Environment

David Reiss, M.D., Robert Plomin, Ph.D., and E. Mavis Hetherington, Ph.D.

Two recent reviews in the American Journal of Psychiatry *and the* British Journal of Psychiatry *reported on progress in understanding the genetics of psychiatric disorder. Both reviews focused on this progress as a prelude to psychiatric diagnostics and therapeutics based on molecular biology. Neither review recognized that the latest data in behavioral genetics support environmental causes for abnormal development and psychopathology as much as they support genetic causes. Moreover, these genetic data point clearly to a type of environmental cause with central importance: the environment that is specific or unique to each sibling in a family.*

(Am J Psychiatry 1991; 148:283–291)

In 1989 the *American Journal of Psychiatry* and the *British Journal of Psychiatry* separately published optimistic articles summarizing recent advances in genetics and their application to psychiatry. Both emphasized the new vistas opening to psychiatry from recent advances in genetic techniques, particularly those which identify specific genetic and molecular mechanisms of disease.

Writing in the *American Journal of Psychiatry*, Pardes et al. (1) reviewed the current methods of genetic research. They summarized the secure advances both in basic research and in practical applications to diseases affecting mental status, such as Huntington's disease. They frankly acknowledged the problems facing research in the major psychiatric syndromes and, anticipating striking gains in these areas, concluded their review with an analysis of clinical problems in genetic counseling.

In an equally optimistic vein, Mullan and Murray, in the *British Journal of Psychiatry* (2), focused most of their review on manic-depressive illness and schizophrenia. Their review centered on the likely heterogeneity of genetic factors in manic-depressive illness and the variable expressivity of genetic factors in both illnesses. Genetic research, they argued, may permit us to redraw the nosological boundaries of psychiatry by revealing, in the case of manic-depressive illness, the various types of genetic defects that lead to the final common pathology. In the case of schizophrenia, once we identify a gene common to many of those afflicted, we can see what other, related disorders are associated with the same gene. This would constitute a genetic basis for a nosologic group of schizophrenia-like disorders.

Thus, these two reviews were similar. The authors noted current progress in a major area of research in biological psychiatry and took us quickly to two major areas of clinical thinking and practice in psychiatry: counseling and diagnosis. They argued that these two practical domains may soon bear a clear imprint of findings about molecular genetic mechanisms in etiology and pathogenesis. These reviews of advances in genetics were, however, distinctly one-sided. First, they

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focused heavily on single-gene mechanisms for explaining the role of heredity in psychiatric disorders. A broad range of data, not reviewed in either paper, strongly indicate that polygenic mechanisms may play a larger role in shaping variations both in normal behavior and in psychopathology (3). Data supporting the importance of polygenic mechanisms are particularly important in the light of recent failures to replicate early findings of single-gene effects in bipolar affective disorders (4) and in schizophrenia. Second, and even more important, neither review indicated that genetic data are providing a new window on environmental mechanisms. In fact, the genetic data are among the best data we have supporting the importance of environmental mechanisms in both normal and pathological development. Even more intriguing, these genetic data are yielding a clear picture of the types of environmental effects likely to be most important. In this review we focus on these environmental implications of genetic findings.

First, our review presents genetic data that support the importance of environmental mechanisms. Here we focus on two issues. Genetic data support substantial effects of environmental mechanisms on normal and pathological development. Beyond that, genetic data suggest that these environmental effects are different from those typically studied. Most studies of the social environment, for example, examine factors that are similar for all siblings in the same family, such as the impact of social class, neighborhood decay, or marital conflict on the psychological development of children. In sharp contrast, the genetic data suggest that the important environmental factors are those which are different for siblings in the same family. These might include differences in how they are treated by the same parent, differences in peer relationships, differences in school environment, and, when they are older, differences in their marital and occupational experiences. In current research, these influences are termed "nonshared environmental effects."

The second purpose of this review is to summarize the current evidence on these nonshared environmental effects. The genetic data alone do not rule out the possibility that most of these nonshared factors could be biological features of the environment. For example, siblings may differ in the quality of the intrauterine environment or in pre- or postnatal exposure to microbial infection or toxins. We know of no studies that systematically compare siblings' exposures to these biological environmental circumstances. However, an emerging body of research indicates the importance of the nonshared social environments. Thus, our review centers on strategies for research on these nonshared social environments, the evidence indicating the social mechanisms that may increase differences in environmental experience for siblings in the same family, and the early evidence linking specific nonshared experiences with both normal and pathological psychological and behavioral development. As more data accumulate, a review of nonshared biological environments may also be in order.

Third, we will discuss the implications of these emerging data for problems in diagnosis and therapeutics in psychiatry. On the basis of these alternative views of behavioral genetics and its implications, we arrive at conclusions very different from those of Pardes et al. and Mullan and Murray.

GENETIC EVIDENCE FOR EFFECTS OF ENVIRONMENT

Magnitude of Effects

As the research in molecular genetics has gathered momentum, it has partially broken loose from its original moorings. The search for specific genes in unipolar, bipolar, and schizophrenic illness began with the demonstration of *significant* genetic effects, but not *exclusive* genetic effects, for both disorders. That is, bipolar and related illnesses occurred among family members of probands with these illnesses more frequently than in the general population, concordances were generally higher in monozygotic twins than in dizygotic twins, and, in studies with the most rigorous designs, the frequency of the illness was higher in biological than in adopted relatives. The same patterns hold for schizophrenia. What is often forgotten is that although the evidence for a genetic contribution to the etiology of these disorders is beyond dispute, no studies indicate that genetic effects account for all the variation between ill and not ill individuals.

For schizophrenia, some older studies showed concordance rates among monozygotic twins as high as 69% and concordance rates among dizygotic twins less than half as high (5). Later studies, with more representative samples and better diagnostic efforts, have yielded much lower concordance rates for monozygotic twins (6, 7). While there remains considerable dispute in weighting environmental and genetic factors, the relatively low concordance rates for monozygotic twins, genetically identical pairs, are powerful evidence for the strong and independent role of the environment in pathogenesis. According to the twin data, the environment may have a direct pathogenic role of its own or may protect individuals from developing disorders to which they are genetically vulnerable.

The picture is less clear for affective disorders. For example, twin studies suggest a stronger role for genetics in bipolar disorders than in schizophrenia (8). These same data suggest an important but smaller effect of genetics on unipolar disorders. Adoption studies—while confirming the heritability of bipolar and unipolar disorders—suggest a less important role for heredity in both forms of affective illness (9). Recent small-sample studies of a variety of disorders beginning in childhood or adolescence yield a similar picture of a balance between genetic and nongenetic causes (10). These disorders include autism, anorexia nervosa, attention deficit disorder, and delinquent behavior.

Using these same data, investigators have been quick to emphasize both the statistical and clinical significance of the genetic effects. What needs additional emphasis is the magnitude of environmental effects—for many conditions they exceed the genetic effects. Thus, to keep current research on the etiology and pathogenesis of mental disorder firmly moored to the fundamental data in the field, a parallel and equally important research program must be undertaken: the most recent findings in behavioral genetics indicate that the discovery of environmental mechanisms clearly has the same importance as the discovery of molecular-based genetic mechanisms.

Nonshared Environmental Influences on Siblings

Behavioral genetics not only estimates the importance of environment in healthy and pathological development but also yields strong clues as to what kinds of environmental effects are most important. The field was given impetus by a landmark study of the heritability of personality by Loehlin and Nichols (11). They studied variation in a number of personality dimensions and in other measures of abilities and values among 514 monozygotic and 336 dizygotic twin pairs drawn from all high school seniors taking the National Merit Scholarship examination. Averaging across a broad range of personality measures, Loehlin and Nichols found the correlation was 0.50 for monozygotic twins and 0.28 for dizygotic twins. Doubling this difference directly yields a heritability estimate of 44%. This means that for personality, at least half of the variance among individuals in this sample was accounted for by environmental factors. However, Loehlin and Nichols drew attention to a curious finding: the monozygotic twin correlations for a broad range of personality variables was only 0.50. This means that of the total variance among twins, about one-half was accounted for by nongenetic factors. Nearly all the effects of the environment were of this nonequivalent, or nonshared, kind. Similar findings have been obtained from studies of many other areas of development. For example, a series of subsequent twin studies showed the importance of nonshared environment for other dimensions of personality (12) and for intelligence (13).

The importance of the nonshared environment in psychopathology has been confirmed repeatedly. Two groups of data are most important. The first are the modest concordance rates for monozygotic twins in most recent studies. For schizophrenia, Gottesman and Shields (7) estimated a concordance rate of 46% by averaging the data from studies reported before 1982. A later study, using precise diagnostic criteria, confirmed this estimate (14). As already noted, concordance was higher in some studies of bipolar patients but is probably lower for unipolar disorders (8).

A second important type of information is concordance rates in siblings. These are upper estimates of the importance of the shared environment. Siblings share the same family, neighborhood, and social class. Thus, shared experiences from any of these sources, which are also important for development, should lead to high levels of similarity in outcome. For schizophrenic and bipolar disorders, the rates of concordance between siblings are 10% or less (7, 15). Concordance rates for adopted siblings, who share no genes, provide a more exacting test of the effects of shared environment; here, similarities could only be explained by common or shared environmental influences. Such studies have not been performed with subjects who have serious psychopathology, although the data from studies of adopted siblings (16, 17) suggest that even the low concordance rates for biological siblings are due to genetic similarity, not shared environment.

THE NONSHARED ENVIRONMENT

Research Strategy

In their first explorations of the nonshared environment, researchers are recognizing three logically ordered steps for identifying these effects. First, the actual differences between siblings for any environmental variable must be determined. Second, the relationship of these differences, if they are observed, to simple family structural variables must be assessed. Third, the role of genes in these differences must be determined. All of these require using at least two siblings in each family recruited into the study. Although sibling studies have been common in genetic research, they are rare in environmental studies.

Social environment. Although differences between siblings in normal and pathological outcomes are beginning to be delineated, we know far less about environmental differences between them. The genetic data suggest that only environmental variables that are significantly different between siblings in the same family are likely to be important in developmental differences. A logical first place to look is differences between siblings in the same family in their relationships with their parents. The preliminary evidence on this topic, however, has not produced consistent findings. Some data have suggested a surprising consistency in parental treatment of children in the same family. For example, in one study (18) investigators directly observed the positive and negative behaviors mothers showed to each of two children in their families. Across families, the behavior shown toward one child was correlated with the behavior shown to the other child. For positive behavior in same-sexed dyads the correlation was 0.82 and for negative behavior it was 0.52. Somewhat higher correlations were obtained in a longitudinal study of mothers and their young children (19). Each mother had two children, 3 years apart in age. During the first phase of the study the mother was observed interacting with the older child, and 3 years later she was observed with the younger child, then the same age as the older child had been during the first observation. Late-adolescent siblings (20) and adult twins (21) reported little difference in how they were treated as children by their parents. However, in one recent study direct observations and self-reports of mothers of preschool children suggested differences in their treatment of their two children (22).

The findings on treatment by siblings contrast with those on parental treatment. Self-report data suggest that one sibling in a family will see himself or herself as being treated by a cosibling differently from how the cosibling sees himself or herself being treated by the sibling (21, 23, 24). However, here too there is also some contradictory evidence. A study of siblings who were 4 and 7 years old showed fewer differences in how siblings treated one another than differences in how the mothers treated these siblings (22).

Finally, two studies have investigated differences between siblings in the characteristics of their peer groups. In one study (23), adolescent siblings saw their peer groups as dissimilar; the magnitude of the dissimilarity of those ratings matched that of the difference in their perceptions of their own relationship with each other. In a study of adult twins (21), another picture was seen: the differences in siblings' perceptions of each other's peer groups were smaller than those for sibling relationships and were about the same magnitude as differences in perceived parental treatment.

Thus, the preliminary evidence suggests that differences between siblings in their perceived treatment of one another are clear and distinct across the life span. Parenting differences are more uncertain, and we have too few data for even a preliminary estimate of the magnitude of differences in peer relationships.

Family structural variables. Once we discover reliable and distinct differences in environment between siblings, we must inquire about the causes of these differences. In particular, we want to know whether they are attributable to such features of the family structure as birth order, age spacing, and gender. If the correlation between the nonshared variable and any of these structural variables is high, then it is important that these structural variables be studied directly. Preliminary data suggest only a few scattered findings of this kind, and these are restricted to nonshared sibling relationships. For example, younger siblings are more likely to envy their older cosiblings, and older siblings do more caretaking of cosiblings than do younger siblings (20). Sensitive multiple regression models are now available to detect these effects, but thus far there have been few such studies (C.L. Slomkowski et al., unpublished data, 1990).

Genetic influences. Siblings may be treated differently because there are differences between them in genetically shaped features of their behavior and responsiveness. Starting with the influential analyses of Bell (25), there has been a great deal of evidence on the ability of even very young children to shape the interaction processes of their families (26). In searching for strong nonshared environmental influences, we would study those which show relatively little genetic influence. Then any association between differences in environment and variation in outcome could not be due to genes but would have to be a main effect.

Genetic influence on the nonshared environment is examined by comparing differences in siblings' environments, by means of direct observation or self-report, in pairs of siblings who differ in genetic relationship. For example, we can compare monozygotic and dizygotic twins or biological and adoptive siblings or full, half, and blended siblings. A genetic effect is presumed if environmental differences are less for sibling pairs who are more similar genetically. To our knowledge, there have been only two studies in which genetic influences on nonshared environmental variables were searched for systematically as part of a search for nonshared environmental influences. In a study of older adolescents, differences in self-reported environments of biological siblings were compared to those of adoptive siblings (20). For most measures, the differences were negligible, suggesting little genetic effect. However, a more recent study of adult twins (21), using the same self-report measures, showed more evidence of genetic effects on these measures: monozygotic twins' reports showed consistently less difference than those of dizygotic twins. For example, substantial genetic effects were observed for the characteristics of the siblings' peer groups: their college orientation, their popularity with others, and their level of delinquency. These data suggest that youngsters may pick their peer groups according to their own heritable characteristics. Although this heritable characteristic has not as yet been identified, these data may exemplify the process of genetically influenced "niche picking," described by Scarr and McCartney (27).

Once an environmental variable has passed these tests, it becomes a candidate in the same sense that specific genetic loci become candidates for monogenic effects on illness after passing through a series of logical elimination steps (1). Two further steps are necessary, however. First, the association of the nonshared environmental variable with variation in developmental outcome must be determined in cross-sectional studies. Then, data from longitudinal studies must demonstrate that variation in the nonshared environmental variable occurs before variation in the trait or syndrome under investigation.

These three steps for identifying candidate environmental variables are being followed systematically in a comprehensive study we are conducting (28). That study focuses on the impact of the nonshared environment on both competence and psychopathology in adolescents. We have assembled a unique group from across the country of 719 families with same-sexed adolescent siblings, typically no more than 2 years apart in age. The families are equally divided into families with monozygotic twins, families with dizygotic twins, families with blended siblings (no genetic relationship), families with half siblings (25% genetic relationship), families with full siblings (50% genetic relationship), and a comparison group of families without divorce. This selection of families permits direct estimates of the correlation of outcome and environmental variables between siblings in the same family, controls for gender effects, and allows for powerful assessments of genetic mediation.

Origins and Impact

The effects of nonshared environments may begin early in life. First may come differences in parental treatment, followed by differences in how siblings treat each other. As maturation proceeds, differences in experiences with peers, schools, and marriage may play important roles. What factors in the family organize and initiate these differences between siblings, and which of these differences influence development?

Environmental differences. Preliminary research suggests that differences between siblings may arise from social processes in two core relationship systems in the family: the parental marital relationship and the sibling relationship. In particular, data suggest the importance of how these dyads manage conflict.

In the marital relationship, conflict is frequent; what distinguishes satisfying from unsatisfying marriages is the facility with which conflict is resolved (29). In marriages where conflict is prolonged and dissatisfaction is high, there are two mechanisms by which this conflict may lead to the creation of different environments for children in the same family.

The first mechanism is a direct one. Studies suggest that a partner who finds the marriage unsatisfying or stressful may single out one child for harsh treatment. For example, in one study of families with distressed marriages the mother, but not the father, typically singled out one child for particularly aversive interchanges (30). Other studies suggest that marital dissatisfaction may also influence fathers' parenting.

Marital conflict may lead to differences in sibling environment by a second mechanism, which involves conflict between siblings themselves. There appear to be two sequential aspects of this second mechanism. The first aspect is the effect of the marital relationship on sibling relationships. Evidence suggests that in families where there is persistent marital conflict there may also be conflict between the siblings (31, 32). Some data suggest that this relationship may depend on the ages and genders of the children and, in many cases, may be mediated by how parents in conflict with each other treat the siblings (33). The second aspect of the mechanism is the link between sibling conflict and the development of the nonshared environment. For example, several studies suggest that a long-term resolution of persistent sibling conflict is a process of "deidentification." Overt conflict may subside over time but be replaced by more covert sibling rivalry, which siblings often have difficulty acknowledging (34). Persistent rivalry is often manifested by siblings who are developing conceptions of themselves that they feel are distinct, if not opposite, from how they regard each other (35, 36). Another example of how sibling conflict turns into nonshared family experience is "split-parent identification." Here, rivalry between two siblings is resolved by each sibling's developing a self-concept like his or her perception of one parent and perceiving the other sibling as resembling the other parent (37). These split-parent identifications may accentuate the special aversive or overly involved relationships that characterize parent-child relationships in conflict-laden families.

Differences in how siblings perceive themselves may lead to differences in how they treat one another. The available data suggest that these differences may be an important component of the nonshared family environment. For example, consider a family with two siblings in which one sibling is aggressive and the other is passive. The former experiences passive sibling behavior, whereas the latter experiences aggressive sibling behavior; the sibling environment for the two siblings is distinctly nonshared.

Nonshared parental and sibling experiences. By whatever social mechanism nonshared parental and sibling effects are produced, studies suggest that both influence normal and pathological development. In studies of parenting differences, the youngest subjects studied thus far (22) were 4 years old; their oldest siblings were 7, and the study focused on differences between siblings in the mother's parenting. In this study, children who received more maternal affection than their siblings were less likely to show depression or related "internalizing" symptoms. However, children who received more control from their mothers were more likely to show these disturbances. The oldest subjects studied so far were adults with a mean age of 35 (21). In that study, the same relationship between maternal control and depression was observed, although the investigators relied on the subjects' memories of how they were treated during childhood and adolescence. In two studies of the nonshared environment and adolescent development (20, 38), different relationships for fathers and mothers were observed. For example, in one study of older adolescents and young adults (38), subjects who reported being controlled by their fathers more than their siblings reported less emotional distress; the same effect did not hold for differences in mothers' control. In contrast, subjects who reported more affection from their mothers had higher educational and occupational aspirations, and the same relationship was true for differences in fathers' affection.

Nonshared experiences involving the sibling relationship also seem important for development. In the same study of older adolescents and young adults (38), the effect of differences between siblings in their treatment of one another was stronger than the effect of differences in parental treatment. However, in another study of 4–7-year-olds (22) the effect of differences in parental treatment was stronger. Certain perceived differences between siblings have emerged as potentially important across studies, ages of subjects, and outcomes. For example, consider differences between the sibling who reports he or she more often took care of the cosibling and the sibling who reports less caretaking. Young adults who reported they did more caretaking had lower scores on a measure of fearfulness than their cosiblings who had less caretaking responsibility (38), and older adults who did more caretaking had higher scores on self-ratings of masculine traits (21). Likewise, differences in feelings of jealousy and inferiority also seem important. Twins who report more jealousy and feelings of inferiority in relation to their co-twins have higher scores on measures of strong affective responses (21) than do their less jealous co-twins; this relationship has also been noted for anger among nontwin siblings (38).

Sequential relationship of nonshared environmental influences. The data we have reviewed focus on nonshared variables that may play a role relatively early in the development of either psychological competence or psychopathology. However, nonshared influences may operate throughout the life of the individual. Moreover, experiences early in life may increase the probability that the individual will be exposed to other nonshared experiences later.

For example, data reported by Bennett et al. (39) suggest a sequence of nonshared experiences that may protect some siblings in a family, but not others, from becoming alcoholic when one or both parents are alcoholics. Early in life the sibling who will grow up free of alcoholism is protected from alcohol by the family group; the family keeps the family practices most cherished by the child free from intrusion by the alcoholic behavior. For example, the family keeps the child from experiencing the parental alcoholism during the child's treasured family Christmas celebration. Later, when these protected children are capable of more self-directed action, they protect themselves from the influences of the alcoholic parent by distancing themselves from the family altogether. Still later in life, the protected and distancing child marries a person who not only has no alcohol problem but does not have a parent who drinks heavily, either. The sequence of these experiences, unfolding over time, may have a strong, cumulative protective effect.

This protective sequence has almost a mirror image in the delinquency and substance abuse career outlined by Patterson et al. (40). Preliminary data suggest that a child destined for serious delinquency and substance abuse is, in early childhood, exposed to a series of coercive exchanges with his or her mother, siblings, and—to a lesser extent—father. These appear to lead to noncompliant behavior at home and school, poor academic performance, and rejection by peers. Later, low self-esteem and even depression develop in many of these children and, combined with the rejection of academically oriented peers, lead them to become members of delinquent gangs and, as a result, to be at risk for a life of delinquency and poor work performance. This sequence has been supported by data from two cohorts of families studied longitudinally (40).

Patterson et al. did not directly compare the experiences of siblings within the same family. However, two studies that did compare siblings (21, 38) confirmed the importance of peer relationships as major correlates of sibling differences in development. For example, siblings who reported that their peers were more college oriented than their cosiblings' peers also showed evidence of greater self-regulation of emotion and greater educational and occupational aspirations. Siblings who reported their peers as very popular with others themselves showed evidence of greater sociability.

Limitations in the Data

The exploration of the nonshared environment is preliminary. Indeed, significant work in this area has only been published during the last 5 years, and the first major studies in the field are just getting under way. Psychiatrists, in particular, will want to know much more about the nonshared correlates of clearly delineated psychopathologic syndromes and nonshared correlates of characteristics of children, adolescents, and adults that clearly protect them against psychopathology, such as self-esteem, social skills, and sustained school and occupational achievement. Both of these needs are being directly addressed in the twin and stepfamily study we are conducting. Moreover, as this field progresses, longitudinal data clarifying the causal role of these nonshared variables will be essential.

GENETICS: A RORSCHACH TEST FOR PSYCHIATRY

We are at just the earliest stages of exploring the environmental implications of the new data from behavioral genetics. The same may be said for the search for molecular genetic mechanisms. Because of their current ambiguity, the data on genes and psychiatry constitute a telling Rorschach test for our field. Seeking to establish itself as a full-fledged biomedical specialty, psychiatry has been quick to see in these genetic data the promise of explanations for psychiatric pathogenesis stemming from single-gene defects, a diagnostic system built around these monogenic causes, and a branch of therapeutics guided by findings, not yet in hand, on molecular genetics. This highly focused enthusiasm is typified by the two recent reviews to which this paper is a response. On the basis of the alternative perspective we have just presented we wish to comment on the concepts of diagnosis presented by Mullan and Murray (2) and of therapeutics suggested by Pardes et al. (1).

Nosology Based on Monogenic Effects

In their review, Mullan and Murray concluded that "the pattern emerging is one of discrete genetic lesions predisposing a core of family members with the defect to the same psychotic illness. . . . It seems that we are about to move into a period when genetics will define disease entities in psychiatry." While this development would provide a welcome simplification and precision in psychiatric diagnostics, it may never come to pass. Mullan and Murray and Pardes et al. allowed for the possibility of environmental causes of bipolar and schizophrenic illness, but they sequestered this possibility by using the concept of "phenocopy." This means that environmental causes, acting without genetic influences, may produce a copy or imitation of the genetically based disorders. An analogy might be diabetes created by surgical removal of the pancreas (the unusual, environmental cause), which is a "copy" of the more ordinary diabetes, which is produced by genetic factors. One might note in passing that the term "phenocopy" is a somewhat prejudicial term, implying that the basic or central disorder is produced by genes and that environmental factors produce copies or imitations. Logically, the antonym "genocopy" might also be used with equal precision in this form of discourse.

Terminology aside, a logical extension of Mullan and Murray's analysis is the vision of a *Diagnostic and Statistical Manual* of the future containing the entries "Schizophrenia, genetic (defect at locus *x*)," "Schizophrenia, genetic (defect at locus *y*)," and "Schizophrenia, environmental." The evidence we have presented here is entirely consistent with, but does not prove, an alternative. It is possible that genetic and nonshared environmental factors operate together to produce the major psychoses (and other important psychiatric disorders) for almost all patients. We have already outlined possible mechanisms by which nonshared environmental factors may operate as important main effects on psychological development. If a syndrome is produced by some balance of genetic effects (monogenic or polygenic) and environmental effects, a diagnostic manual would contain few if any entries based exclusively on genetic knowledge.

Gene-Based Psychotherapy

The argument for therapeutics based on genetics, by Pardes et al., seems even more premature. They began their discussion of this point, in the concluding section of their review, by recommending that all psychiatrists acquire a sound knowledge of the principles and current findings in genetics. To this we take absolutely no exception. From this point their argument veered off a course justified by current data. They engaged in an extended discussion of clinical tests for genetic defects that they implicitly recognized are still in the future. "The issues of whom to test diagnostically for genetic abnormalities, when to offer testing, and how to interpret results to patients are laden with ethical as well as *psychotherapeutic* problems" (emphasis added). In their vision of the future of a branch of therapeutics, based on genetic knowledge, Pardes et al. constricted the role of psychological therapeutics to dealing only with the stress of genetic testing. There are simply no data on which to base such a Draconian view. The data we have presented here argue, again, for a strikingly different vision. The genetically informed psychiatrist may be required by emerging data to identify and modify genetic and environmental factors as they shape development. The nonshared environmental effects are likely to operate through a nexus of marital, parenting, sibling, and peer influences in which the psychiatrists' patients, whether they are parents concerned about the risk of disorder or children who have the disorder, play a central role.

After focusing on the stress of genetic testing, Pardes et al. expanded on their vision by imagining situations where ordinary psychiatrists might not be able to cope. "In situations where the practitioner feels that he or she has insufficient expertise to offer genetic *counseling*, the patient should be referred to someone else, preferably to a psychiatrist specializing in these problems" (emphasis added). Given the strong possibility of important roles for environmental variables, acting in concert with genetic variables, we doubt the wisdom of arguing now for a specialized field of genetic counseling in psychiatry (although it is developing nonetheless).

We have, in fact, two serious reservations about this line of professional development. First, if future data support the importance of both genetic and environmental effects in most syndromes and for most patients, the integration of genetics and environmentalism would become a core problem in the training and practice of psychiatrists. Sequestering psychiatric genetic knowledge in a specialized subdiscipline may destroy the opportunities for fully integrated diagnosis and treatment planning. A second reservation concerns the treatment modalities implied by the term "counseling." While Pardes et al. did not make explicit what they meant, commonly accepted definitions suggest this approach would be built around straightforward instruction and support. The key ingredient presumably would be the well-timed and well-phrased conveying of information by the knowledgeable professional to the interested, if not desperate, layperson. However, it is doubtful that this approach could effect the changes in social interactional patterns, or other social environmental variables, that may be necessary to reduce the environmental risk factors for syndromes jointly determined by those variables and genetic processes.

CONCLUSIONS

In sum, the rapidly growing field of behavioral genetics has opened up new vistas for psychiatry. Two companion developments sharpen this image of the future: molecular biology promises a rich harvest of information about specific gene and enzyme defects, whereas comparable advances in the study of the nonshared environment, including human relationships, promise equally important information about environmental contributions to pathogenesis. In effect, Mullan and Murray and Pardes et al. used fragments of data currently in hand, coupled with the promise of a powerful technology, to paint a futuristic picture of psychiatry. We are doing the same. Ordinarily, such portraits can be illuminating or, at worst, harmless. However, psychiatry has always been a precarious discipline. At least since the publication of *Studies on Hysteria* (41), nearly 100 years ago, there have been persuasive arguments that the major psychiatric syndromes cannot be fit neatly into standard biomedical molds. Psychiatry has been forced into the chronically uncomfortable position of straddling biomedicine and the social sciences and seems always to hunger for relief. Psychiatry derives a remarkable portion of its self-image from pictures of its future. For example, images of a psychiatry based on molecular biology, of the kind rendered by Mullan and Murray and Pardes et al., have had an enormous impact on the types of research that currently receive public funding. However, despite its identity problems, psychiatry has matured considerably in this century. Increasingly, its internal disputes are resolved by appeals to carefully collected empirical data. In the present case, the data simply do not permit a conception of the future centered on a straightforward biomedical answer to the fundamental question of the pathogenesis of major disorders. Indeed, a balanced image of the future contains a growing and equal partnership of the social sciences and molecular biology.

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Substance Abuse and Cerebral Blood Flow

Roy J. Mathew, M.D., and William H. Wilson, Ph.D.

Objective and Method: This paper reviews acute and chronic effects of drugs of abuse on cerebral blood flow (CBF) and metabolism and their clinical significance. The most important source of information for the review is human research reports published in refereed journals. A few animal studies, book chapters, and abstracts that are especially relevant are also included. Results: In humans, ethanol in small doses produces cerebral vasodilation; higher doses induce cerebral vasoconstriction. Chronic alcoholism is associated with reduced CBF and cerebral metabolism. Sedatives and antianxiety drugs lead to global reduction in CBF and cerebral metabolism. Caffeine, even in small doses, is a potent cerebral vasoconstrictor. Cerebral vasodilation is seen immediately after cigarette smoking, but chronic smokers show global reduction in CBF. Changes in CBF after marijuana smoking are variable; both increases and decreases are seen. Chronic marijuana smoking, however, seems to reduce CBF. Most inhalants and solvents are vasodilators; chronic abuse is accompanied by a decrease in CBF. A number of drugs of abuse, including ethanol, amphetamines, cocaine, nicotine, and caffeine-phenylpropanolamine combinations, increase the risk for stroke. Reduction in CBF associated with chronic use of ethanol, nicotine, inhalants, and solvents is at least partially reversible upon abstinence. Conclusions: Topics for future research include regional brain function, which mediates drug-induced mood changes (euphoria); CBF concomitants of psychological and physiological characteristics that increase addiction potential; changes in CBF that accompany withdrawal syndromes; mechanisms responsible for drug-induced stroke; and effects of functional and organic complications on CBF.

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Cerebral blood flow (CBF) research is important in relation to substance abuse disorders for a variety of reasons. Among the most important of these is that drugs of abuse induce behavioral changes that in all probability are related to altered brain function. In the structurally intact brain, CBF and cerebral metabolism are closely coupled with brain function (1). Thus, drug intoxication and withdrawal are likely to be accompanied by changes in CBF, i.e., brain function. Long-term drug abuse leads to various neuropsychiatric and cerebrovascular complications that are likely to be associated with altered CBF. In spite of an impressive number of research reports, this topic has received only a little attention in psychiatry.

DRUG-INDUCED CHANGES IN CBF: MECHANISMS

Acute Pharmacological Effects

Drugs, including substances of abuse, can influence CBF through several mechanisms. Changes in brain function and blood gases and cerebral vascular effects seem to be the three most important mechanisms responsible for the acute effects of drugs on CBF. Since CBF is closely coupled with brain function, drug-induced changes in the latter are accompanied by parallel changes in the former (1). Drug-induced changes in mood and behavior are probably associated with alterations in brain function, and drugs may differ with respect to the site and direction of these alterations. CO_2 is a potent cerebral vasodilator (2–4), and drugs usually increase and decrease CO_2 levels by influencing respiration. A number of pharmacological agents act directly on the cerebral vasculature.

There are a few other less well known mechanisms. A number of vasoactive neuropeptides, which coexist with neurotransmitters in synaptic vesicles, are inti-

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mately related to the behavioral effects of addictive drugs (5). Blood viscosity has an inverse correlation with CBF (3, 4–6); however, none of the substances of addiction (with the possible exception of ethyl alcohol) are known to induce changes in viscosity. Cerebral blood vessels are innervated by autonomic fibers and by brainstem nuclei by means of axons that come up through the brain parenchyma (intraparenchymal innervation) (3, 7, 8). The role played by autonomic nerve fibers in drug-induced changes in CBF is an important but not well understood topic. There is an impressive volume of literature on the effects of neurotransmitters on CBF (7).

Long-Term Effects and Complications

The long-term effects of drugs on CBF involve other mechanisms. These include endocarditis with embolism, direct toxic injury to blood vessels, embolization of foreign material (e.g., adulterants), pharmacological alteration of vascular function (e.g., cocaine-induced increase in blood vessel sensitivity to epinephrine and norepinephrine), and immunogenic vascular injury (e.g., vasculitis) (9). Functional psychiatric disorders are associated with altered CBF (10), and a wide variety of syndromes such as mood disorders, psychotic reactions, and confusional states occur secondary to substance abuse. A number of drugs of abuse, including alcohol, cause morphological changes in the brain (11). Brain atrophy is usually accompanied by reduced CBF; the degree and location of the decrease in CBF depends on the site and extent of brain tissue loss (12). Last, physical complications of substance abuse that result in changes in blood viscosity (e.g., anemias), hypertension, alterations in blood CO_2 and oxygen levels (e.g., emphysema associated with tobacco smoking), and accumulation of vasoactive toxic substances in the blood (e.g., liver disease due to alcohol) can lead to considerable alterations in CBF (13).

TECHNIQUES FOR MEASUREMENT OF CBF IN HUMAN SUBJECTS

The first quantitative technique for measuring CBF, developed by Kety and Schmidt (14), involved inhalation of subanesthetic concentrations of nitrous oxide and repeated sampling of the internal jugular and arterial blood. With this method, which used a modification of the Fick principle, CBF and cerebral metabolism in the entire brain were computed. Ingvar and Lassen (15) developed a technique based on intracarotid injection of a radioactive substance and computation of regional CBF values for the ipsilateral region (supplied by the internal carotid artery) from the progressive decline in scalp radioactivity recorded by externally applied, stationary scintillation detectors.

Obrist et al. (16) developed a totally noninvasive technique in which inhalation replaced intracarotid administration of the isotope (xenon-133 inhalation technique). Xenon-133, a gamma-emitting gas, was mixed with room air and administered through a face mask for 1 minute, after which radioactivity over the scalp was recorded for 10 minutes with scintillation detectors mounted on a helmet and applied to the scalp. These scalp clearance curves were analyzed by using a bicompartmental model with corrections for contamination of CBF by extracranial flow, the recirculating radioisotope, and radioactivity of the respiratory passage. The fast-clearing compartment yielded gray matter perfusion rates. The technique measured CBF to both hemispheres and in regions supplied by both the carotid and vertibrobasilar arterial systems.

The techniques of Ingvar and Lassen and Obrist et al. measure only cortical flow. Three-dimensional techniques such as single photon emission computed tomography (SPECT) (17) and positron emission tomography (PET) (18) measure subcortical as well as cortical flow. The latter, which is the most technologically sophisticated and expensive method, also quantifies cerebral metabolism and can provide information on receptor mechanisms.

ETHYL ALCOHOL

Intoxication

Most of the in vivo studies of rats, cats, and dogs have concomitantly used drugs with sedative properties and drugs with vasoactive properties, which could probably account for the wide variations in the results reported (19–25). Thomas (25) noted dilation of the pial vessels that lasted up to 30 minutes in awake and anesthetized cats and rabbits given intravenous or intracarotid injections of ethyl alcohol. Friedman et al. (23) found a generalized decline in CBF, especially cerebellar CBF, in awake dogs after they were given ethanol. Barry and associates (21, 22, 24) reported increases in CBF at low blood alcohol levels and reduced CBF and cerebral oxygen metabolism at higher levels. Comparable findings were also reported by Hadji-Dimo et al. (19). Roach and Reese (26) showed that acute alcohol intoxication decreased utilization of brain glucose. Altura et al. (27–29), using a rat brain preparation, demonstrated graded contractile responses in cortical arterioles and venules at ethanol concentrations of 10–500 mg/dl. Regardless of whether ethanol administration was intravenous, intraperitoneal, intracarotid, or perivascular, higher concentrations of alcohol caused irreversible spasms often followed by rupture. These investigators also reported similar findings in studies that used isolated canine cerebral and basilar arteries.

Goldfarb et al. (30) found reduced differences in oxygen in arterial and jugular vein blood (indicating reduced cerebral oxygen metabolism) in patients hospitalized while intoxicated. Loman and Myerson (31) found inconsistent changes in cerebral glucose and oxygen metabolism during intravenous infusion of 50–85 cc of absolute alcohol as a 5% solution. Hine et al. (32), using the Kety-Schmidt technique, found modest but statistically significant decreases in CBF and cerebral metabolism 20 minutes after subjects ingested 90-proof whiskey (0.5 ml/kg of body weight). The authors, however, pointed out that in spite of the statistical significance, the changes were very inconsistent.

Battey et al. (33) measured CBF with the same technique before and during the intravenous infusion of 5%–10% solutions of ethanol in 15 patients convalescing from a variety of medical illnesses. Patients who were brought to the hospital emergency room with severe alcoholic intoxication were also studied. Measurements were performed 1–2 hours after admission and 15–24 hours later, when the patients were sober. During alcohol intoxication, with high blood levels (0.3 mg/dl), there was a pronounced increase in CBF and reduction in cerebral oxygen metabolism and cerebrovascular resistance.

Sutherland et al. (34) could not demonstrate any changes in CBF or cerebral metabolism following the oral administration of 1 mg/kg of ethanol. Miyazaki (35) studied changes of internal carotid and brachial artery flow with an ultrasonic Doppler technique after subjects drank 2 ml of absolute alcohol in 20 ml of water. No alterations in either arterial flow were found in 41.7% of the subjects. While 25% of the subjects showed a slight increase in internal carotid and brachial flow, another 25% showed a conspicuous increase in internal carotid artery flow with no changes in brachial flow. A few subjects (8.3%) showed a conspicuous increase in peripheral circulation with no alteration in cerebral circulation.

More recently, Newlin et al. (36), using the xenon-133 inhalation technique, measured CBF 1 hour after oral administration of 0.75 g/kg of alcohol. Control measurements were made in the same subject, under resting conditions, on the same day or a different day. Alcohol intoxication was associated with a global increase in gray matter flow. This increase was bilaterally symmetrical in the posterior regions, but the right anterior region showed more pronounced change than the corresponding area on the opposite side.

We measured changes in regional CBF with the xenon-133 inhalation technique during ethanol intoxication (0.5 g/kg) in 14 (and after placebo in 12) physically and mentally healthy subjects who had been drug free for a minimum of 2 weeks (double-blind study) (37). Postethanol CBF, after correction for CO_2 level, showed a bilateral global increase.

Volkow et al. (38) used ^{15}O-labeled water and PET to examine the effects of 0.5 g/kg and 1 g/kg of ethanol on CBF in 13 normal social drinkers. Both doses of ethanol reduced blood flow to the cerebellum, although it was significantly reduced only at the high dose. The high dose increased blood flow to the right temporal and prefrontal cortex, especially 60 minutes after ethanol was given.

Two recent studies evaluated ethanol-induced changes in cerebral glucose metabolism with [^{18}F]2-fluoro-2-deoxy-D-glucose and PET. The study by de Wit et al. (39) measured cerebral glucose metabolism after a placebo and after 0.5 g/kg and 0.8 g/kg of ethanol in eight healthy male volunteers during three visits to the laboratory at 7-day intervals. While the low dose of ethanol produced nonsignificant, variable changes, the high dose decreased global cerebral glucose metabolism significantly; regional differences were not striking. Volkow et al. (40) measured cerebral glucose metabolism under baseline conditions and after 24 hours of ethanol administration (1 g/kg) in six normal subjects and six alcoholics. After ethanol, cortical and cerebellar glucose metabolism decreased, with minimal changes in the corpus callosum and basal ganglia. The alcoholics showed the more pronounced changes.

Berglund et al. (41) reported an increase of 30%–60% in CBF in a 61-year-old man during an alcoholic blackout (blood alcohol level=0.38%), as compared to findings of repeated studies in the same man during abstinence.

The animal literature on this subject is inconclusive. Most human studies suggest that cerebral vasodilation occurs with small doses of alcohol and that higher doses produce cerebral vasoconstriction. The confusion in the literature can be explained by differences in the types of subjects studied and the doses of alcohol used.

It is important to note that ethanol can produce CBF changes in opposite directions through different mechanisms. Ethanol is a well-known cerebral depressant and, like other sedatives, it should reduce CBF as a result of its effect on brain function. PET scan studies showing reduced glucose metabolism after ethanol support this possibility. However, in small doses, ethanol has a disinhibiting effect that may produce an increase in CBF, at least in certain brain regions (subcortical). Alcohol is vasoactive and induces vasodilation in the periphery (42); such a mechanism may also be operant in the cerebral vascular bed. Acetaldehyde is a vasodilator (32), and individuals differ in the amount of acetaldehyde produced after a standard dose of ethanol (43).

Withdrawal

Eisenberg (44), using the Kety-Schmidt technique, found a reduction in CBF and cerebral oxygen and glucose metabolism in six patients with delirium tremens. Marx et al. (45), using the same measurement technique, studied cerebral metabolism and CBF in seven patients who had mild alcoholic delirium (without hallucinations or confusion), another seven patients who had acute delirium tremens (with hallucinations and confusion), and nine patients who were free of delirium. They were unable to demonstrate statistically significant differences in CBF or cerebral metabolism among the three groups. Berglund and Risberg and associates (46, 47) made serial bilateral CBF measurements with the xenon-133 inhalation technique during 13 withdrawal periods in 12 male alcoholics. They found a significant reduction in global CBF, which was most marked in patients with clouded sensoria and after an extended binge, during the first 2 days of withdrawal. Auditory and visual hallucinations were associated with elevated CBF in temporal, parietal, and occipital regions. They found an inverse correlation between degrees of confusion and CBF.

Hemmingsen et al. (48) measured regional CBF with xenon-133 and SPECT in 12 alcoholics during withdrawal before and after barbital treatment. Measurements were obtained at a similar interval in 10 normal subjects. The alcoholic patients were subdivided into three groups at the time of admission: those with hallucinations and agitation (N=4), those with hallucinations without agitation (N=4), and those with no hallucinations or agitation (N=4). The first group showed significantly higher CBF than the other two groups during the first measurement. CBF after withdrawal was significantly lower for the first two groups. None of the pre- or postwithdrawal CBFs differed significantly from the control values. The values were adjusted for blood alcohol concentration and CO_2 level. Psychomotor agitation was significantly correlated with CBF, but hallucinations and confusion were not. The small number of subjects in each subcategory raises questions about the validity of the results.

Campbell et al. (49) studied glucose uptake with [^{14}C]2-deoxy-D-glucose and autoradiography in rats during ethanol withdrawal syndrome. There was a general increase in glucose uptake, which was most pronounced in the sensorimotor cortex, globus pallidus, thalamus, and cerebellum.

The variability in CBF during withdrawal is not surprising in view of the multiplicity of withdrawal symptoms and variations in severity from patient to patient. In most cases, there seems to be a decrease in CBF; however, an increase is seen in hallucinating and agitated patients.

Long-Term Effects

Rogers et al. (50) used the xenon-133 inhalation method to study the relation between social drinking and CBF in 218 normal volunteers divided into four groups according to their average alcohol intake during a 5-year period. They found a progressive reduction in CBF that was inversely correlated with the amount of alcohol consumed, even after the CBF values were adjusted for the presence of risk factors for cerebrovascular diseases, such as hypertension, hyperlipidemia, heart disease, and diabetes. Shimojyo et al. (51) found a 36% reduction in CBF and cerebral metabolism during the acute stages of Wernicke-Korsakoff encephalopathy, which persisted for 5–28 days after abstinence. Reduced CBF and cerebral metabolism in acute Wernicke-Korsakoff syndrome were also reported by Headlund et al. (52) and Kruger and Hoyer (53). Simard et al. (54) and Berglund and Ingvar (55), using the intracarotid xenon-133 technique, found a large variance in mean CBF in patients with chronic Korsakoff psychosis. More recently, Meyer et al. (56) reported a decrease in gray and white matter flow, measured with the xenon-133 inhalation technique, in 19 males with acute Wernicke-Korsakoff syndrome and an increase in CBF after abstinence and treatment with thiamine. The same authors also reported reduced gray matter flow (which returned to normal with abstinence) and normal white matter flow in chronic alcoholics without Korsakoff's syndrome (57).

Samson et al. (58) measured cerebral glucose metabolism with [^{18}F]2-fluoro-2-deoxy-D-glucose and PET in six neurologically normal primary alcoholics (four men and two women) and in age-matched control subjects. They observed a nonsignificant trend toward decrease in glucose metabolism in most cortical regions in the alcoholics. In subcortical regions and the cerebellum, the metabolic rate was very similar in the alcoholics and the control subjects. When the absolute regional metabolic values were expressed as ratios of the corresponding mean cortical values, the ratio for the mediofrontal region was significantly lower in the alcoholics.

Sachs et al. (59) studied cerebral glucose metabolism, using [^{11}C]2-deoxy-D-glucose and PET, in 10 chronic alcoholics without Korsakoff's psychosis and in 25 control subjects. The alcoholics showed significantly lower glucose metabolism for the entire brain and fewer significant interregional correlations. Unlike the control subjects, eight of the nine right-handed alcoholics did not have an increase in right hemisphere metabolism during a nonverbal auditory stimulus. Kessler et al. (60) reported global reduction in cerebral glucose metabolism, measured with [^{18}F]2-fluoro-2-deoxy-D-glucose and PET, in six alcoholics with Korsakoff's syndrome.

There is some uncertainty about whether all alcoholics with varying degrees of dementia show reduced CBF. In a review, Berglund (61) concluded that the average 30- to 40-year-old alcoholic is likely to have normal CBF values. He pointed out that alcoholics with delirium tremens and hepatic cirrhosis are more likely to have reduced CBF. However, the findings from several other laboratories seem to argue against this conclusion (51–54, 56–60). The findings by Berglund indicating a greater vulnerability of right hemisphere CBF to the effects of chronic alcoholism (61) could not be confirmed by Meyer and associates (56, 57). Chronic alcoholism is associated with white matter lesions (62), and therefore the effect of alcohol on white matter flow is relevant. Unfortunately, the xenon-133 inhalation technique, used by most investigators, does not measure white matter flow adequately (16). With the intracarotid xenon-133 injection technique, Berglund and Ingvar (55) and Johannesson et al. (63) found reduced white matter flow in chronic alcoholics. However, Meyer and associates could find reduction in gray matter perfusion only in Wernicke-

Korsakoff patients (56) and not in patients with alcoholic dementia without Wernicke-Korsakoff syndrome (57).

Clinical Significance

A number of studies ranging from case reports (64) to large-scale studies have consistently pointed to an association between ethanol and stroke, especially cerebral hemorrhage, in young adults (65–72). Acute intoxication immediately preceded stroke in many instances.

The association between alcohol ingestion and stroke can be explained by a variety of mechanisms (73). Alcoholism can lead to hypertension, which is closely related to stroke. Similarly, alcohol can accentuate cardiac arrhythmias and cardiomyopathy, both of which can be related to stroke. Changes in clotting mechanisms and increases in hematocrit and plasma osmolarity are other factors related to excessive alcohol consumption and stroke. Animal studies point to alcohol-induced cerebral vasospasm as a causal mechanism. Increase in CBF following mild to moderate degrees of intoxication, which several human studies seem to suggest, may increase the risk for cerebral hemorrhage after minor head injuries.

Decrease in CBF in chronic alcoholism is most likely due to associated loss of brain tissue. In other types of dementias, reductions in CBF have been reported (52–54). Reversibility of the change in CBF (as well as in cognitive dysfunction) with abstinence and appropriate treatment suggests that part of the decrease in CBF may be due to brain dysfunction.

SEDATIVES AND ANTIANXIETY AGENTS

Acute Effects

Earlier research carried out with the Kety–Schmidt technique consistently pointed to a dose-dependent decrease in global CBF and cerebral oxygen metabolism after ingestion of barbiturates (74). More recent studies on changes in CBF associated with bolus injections of benzodiazepines indicate bilateral decreases. Forster et al. (75, 76) showed bilateral decreases in CBF (unrelated to CO_2 level) and cerebral metabolic rate for oxygen after 0.15 mg/kg of midazolam was given to subjects studied with the xenon-133 inhalation technique. Midazolam-induced decrease in CBF was blocked by concomitant administration of the benzodiazepine antagonist flumazenil (77).

We used the xenon-133 inhalation technique to study the effects on CBF of tranquilization induced with small doses of diazepam (78). CBF was measured before and 5 minutes after slow intravenous administration of 0.1 mg/kg of diazepam (mean±SD=7±1.6 mg) or normal saline given on a double-blind basis. The subjects were specifically instructed to stay awake with eyes open, and none of the subjects became drowsy during the experiment. Five male and five female subjects received diazepam, while another group of five male and five female subjects received saline. Hemispheric CBF corrected for changes in end-tidal CO_2 level showed a significant decrease in the right hemisphere and a nearly significant decrease in the left hemisphere ($p<0.06$). The most significant change occurred in the frontal lobe, especially on the right side.

Indirect sources of evidence indicate that the nondominant hemisphere is the site of action for barbiturates and alcohol, which also induce tranquilization, euphoria, and disinhibition (46, 79). The frontal lobe has dense connections with subcortical structures and has long been associated with arousal and emotions (80). Psychosurgical techniques such as capsulotomy and frontobasal tractotomy, which reduce anxiety and tension, also reduce frontal perfusion (81). It must be noted that frontal lobe lesions and psychosurgery can induce indifference, silliness, euphoria, and disinhibition (82), which are also known to occur following the administration of diazepam, alcohol, and barbiturates. Thus, it is possible that the mood changes induced by moderate doses of these drugs are mediated through suppression of the nondominant hemisphere, especially the frontal lobe. However, the results of our study (78) need to be replicated with a larger number of subjects.

Foster et al. (83) twice measured cerebral glucose metabolism with PET in five patients with probable Alzheimer's disease (mean interval=4.2 months). On the first occasion, measurements were made when the subjects were at rest. On the second, laboratory conditions were identical except that an intravenous injection of diazepam, titrated to maintain stage 2 sleep by clinical and/or EEG criteria, was given. The subjects were arousable with vigorous tactile stimulation but not with spoken words, and the blink response to eyelash stimulation was extinguished. Cerebral metabolic rate for glucose decreased an average of 30% during diazepam administration, and the degree of decrease was dose related. There were no differences between the two hemispheres in diazepam-induced changes. Metabolism in different brain regions changed in an identical manner after diazepam.

Long-Term Effects

Buchsbaum et al. (84) measured cerebral glucose metabolism with PET before and after treatment with clorazepate in 18 physically healthy right-handed patients with generalized anxiety disorder. The patients were randomly assigned to clorazepate (3.75 mg/kg) and a placebo for 21 days, and the drugs were administered in a double-blind design. Metabolism of 12 brain structures (for which human autopsy studies of benzodiazepine receptor binding were available) was analyzed. Greater reduction in metabolism was found in the occipital and frontal cortex, especially on the right as compared to the left. Subcortical structures showed little alteration. Density of regional benzodiazepine binding was significantly correlated with cerebral metabolism.

These studies clearly showed global reduction in CBF and cerebral metabolic rate, with no regional variation, after acute administration of sedating doses of antianxiety agents. However, acute administration of nonsedating doses of benzodiazepines and long-term treatment of anxiety with nonsedating doses of benzodiazepines have produced regional differences. Intravenous administration of nonsedating doses of diazepam produced more significant changes in CBF in the right hemisphere, especially the frontal region. Long-term treatment with clorazepate induced a decrease in glucose metabolism in the occipital and frontal cortex, especially on the right side as compared to the left. The drug seemed to have a minimal effect on subcortical metabolism. No information is available on the effect of benzodiazepine withdrawal on CBF and cerebral metabolism.

STIMULANTS

The physiological and behavioral effects of stimulants have become important along with the increasing popularity of cocaine as a drug of abuse (85). Stimulants increase pulse rate, blood pressure, and autonomic activity. Many of these drugs stimulate the respiratory center and cause hypocapnia. Most stimulants are sympathetic agonists. The multiple mechanisms through which these drugs can influence CBF make study of their effects difficult.

Caffeine

Acute effects. Caffeine is widely used for its CNS-stimulating property. Excessive use of the drug has been associated with anxiety, restlessness, and depression (86). The literature on the effect of caffeine on CBF in animals is inconclusive (87). On the other hand, studies conducted in humans with the Kety-Schmidt technique have consistently indicated a caffeine-related decrease in CBF (88–92). We and our colleagues conducted a series of experiments with the xenon-133 inhalation technique on the effect of caffeine on CBF in human beings which confirmed previous reports of global cerebral vasoconstriction, with no regional variations, after a relatively small dose of the drug (250 mg) (93–96). In older subjects (mean±SD age=64.0±9.4 years) caffeine was not associated with any significant reduction in CBF (95).

Long-term use and withdrawal. Another study evaluated the effect on CBF of chronic caffeine intake and sudden withdrawal (96). Eight subjects who gave a history of consuming more than six cups of coffee daily for a minimum of 3 years (the high-caffeine group) participated in this project. Matched subjects whose daily caffeine intake had been less than three cups for a minimum of 3 years constituted the low-caffeine group. CBF was measured three times in each participant in both groups: 1) before and 2) 30 minutes after the ingestion of 250 mg of caffeine and 3) after 24 hours of abstinence from caffeine. In the high-caffeine group, caffeine ingestion was associated with a significant reduction in CBF. After 24 hours of abstinence from caffeine, the high-caffeine group showed an increase in CBF that reached statistical significance in several frontal regions bilaterally. There were no changes in CBF in the low-caffeine group after 24 hours of abstinence.

These studies clearly show that a small dose of caffeine (250 mg), equal to two cups of drip coffee (86), induced a significant reduction in global CBF that lasted more than 90 minutes. A similar decrease in CBF is seen after ingestion of caffeine even in people who consume large quantities of it. These findings argue against the development of tolerance to a caffeine-induced decrease in CBF. Caffeine withdrawal in consumers of large amounts of caffeine was associated with an increase in CBF. The precise mechanism responsible for the caffeine-induced cerebral vasoconstriction is unclear. The changes in CBF were unrelated to changes in general circulation and CO_2 levels. Similarly, caffeine in a dose sufficient to induce cerebral vasoconstriction (250 mg) did not increase anxiety levels. Caffeine given in low doses has been shown to bind to adenosine receptors in a dose-dependent manner (97). Adenosine is a powerful cerebral vasodilator (97), and therefore adenosine receptor blockade by caffeine would seem to be the most plausible explanation for the reduction in CBF.

Clinical significance. Caffeine-induced decrease in CBF is clinically significant in several ways. Blood is the vehicle through which drugs that act on the CNS reach the brain. Caffeine-induced cerebral vasoconstriction that is sustained after 90 minutes can thus reduce drug delivery to the brain. The reduction in CBF after caffeine intake does not seem severe enough to cause symptoms of cerebral ischemia in normal subjects. However, it is unclear whether it increases the risk for transient ischemic attacks and cerebral infarction in high-risk individuals and in those recovering from cerebrovascular accidents. Over-the-counter diet preparations and illicit drugs that contain caffeine and phenylpropanolamine have been reported to cause confusion, psychosis, seizures, and stroke (98). Phenylpropanolamine-induced hypertensive crisis is generally considered to be responsible for this; cerebral vasoconstriction secondary to intake of caffeine may be an additional contributing factor. Caffeine-induced changes in CBF may also be relevant in dementias that are associated with reduced cerebral perfusion.

Amphetamines

Amphetamines are stimulants well-known for their addiction potential. Research on the effects of amphetamines on CBF has produced conflicting results both in human beings and in animals. Substantial increases in

CBF and cerebral metabolic rate were reported in rats after intravenous administration of amphetamine (99, 100). However, in monkeys, although increases in cerebral metabolism and CBF were seen after intracarotid administration of small doses of amphetamine, large doses caused cerebral vasospasm and decreased CBF (101, 102).

Wechsler et al. (103) used [^{14}C]2-deoxy-D-glucose and autoradiography to study conscious rats given a dose of amphetamine and demonstrated an increase in glucose metabolism in components of the extrapyramidal system (especially the subthalamic nucleus and zona reticulata of the substantia nigra) and a decrease in metabolism in the habenula and suprachiasmatic nuclei. Orzi et al. (104), with the same technique, found an increase in glucose metabolism in the extrapyramidal system in rats after 5 mg/kg of amphetamine was given. Progressive escalation of the dose to 15 mg/kg over 3 weeks resulted in an increase in metabolism in the nucleus accumbens, which the authors felt might have been related to amphetamine psychosis.

Studies with the Kety-Schmidt technique in human beings did not reveal any global changes in CBF or cerebral metabolism after 20 mg of amphetamine were administered (87, 105). More recently, Berglund and Risberg (106) reported a substantial increase in CBF, especially to the left hemisphere and frontal lobes, in an amphetamine addict after he reported that he had ingested the drug (106).

We measured CBF with the xenon-133 inhalation technique before and after intravenous injection of 15 mg of dextroamphetamine sulfate in 10 physically and mentally healthy subjects and after injection of saline in 12 control subjects (107). Amphetamine was associated with a significant increase in blood pressure and a decrease in CO_2. Scores on the Profile of Mood States (POMS) (108) showed postamphetamine increase in vigor. Subjects who received amphetamine showed a trend toward a decrease in CBF that did not reach statistical significance in most brain regions.

Kahn et al. (109) measured CBF with the xenon-133 inhalation technique before and 30 minutes after intravenous infusion of dextroamphetamine (0.3 mg/kg) and saline in 12 right-handed, physically and mentally healthy male volunteers. Postamphetamine CBF showed a significant global decrease, which became nonsignificant when the CBF values were corrected for CO_2 level. Amphetamine was associated with a significant increase in autonomic and behavioral arousal. Wolkin et al. (110) quantified cerebral glucose metabolism with PET after placebo and after 0.5 mg/kg of dextroamphetamine in 10 schizophrenic patients and six control subjects. Both groups showed a generalized postamphetamine reduction in cerebral metabolic rate, which was significant for frontal regions bilaterally and the left temporal region in the control subjects. Plasma amphetamine level was inversely correlated with cerebral metabolism in several regions.

Amphetamine is a stimulant and would therefore be expected to cause an increase in CBF. Thus, the trend toward postamphetamine decrease in CBF is difficult to explain. Correction for CO_2 level did not alter the results. CBF is autoregulated (2–4), and therefore modest postamphetamine increase in blood pressure is unlikely to be the explanation. As was pointed out earlier, cerebral blood vessels receive sympathetic innervation (8), and amphetamine is a sympathetic agonist. Postamphetamine decrease in cerebral metabolic rate suggests a corresponding reduction in brain activity. It is possible that suppression of the cortex, which normally inhibits subcortical centers (80), is involved in inducing feelings of elation and disinhibition. However, Wolkin et al. (110) found reduced subcortical metabolism in subjects given amphetamine. It may be argued that PET scan does not have enough spatial resolution to image various subcortical structures satisfactorily. However, autoradiographic studies of rats support the possibility of increased subcortical activity after amphetamine.

Cocaine

Acute effects. London et al. (111), with the [^{14}C]2-deoxy-D-glucose and autoradiography technique, demonstrated an increase in glucose metabolism in the extrapyramidal system of rats after intraperitoneal administration of cocaine. Porrino et al. (112), using the same technique, found increased metabolism in the medial prefrontal cortex and nucleus accumbens after administration of 0.5 mg/kg of cocaine; the authors argued that this might be related to the reinforcing properties of the drug. A dose of 1 mg/kg produced more widespread increases in cerebral metabolism.

London et al. (113) used [^{18}F]2-deoxy-D-glucose and PET to examine the effects of 40 mg of cocaine hydrochloride given intravenously to eight polydrug abusers in a double-blind, placebo-controlled crossover study. Most brain regions (except the pons and cerebellum) showed decrements in glucose metabolism after the drug was given.

Long-term effects. Volkow et al. (114) compared CBF measured with ^{15}O-labeled water and PET in 20 right-handed male cocaine users (average age=27 years, range=21–34) and 24 healthy, right-handed male volunteers of comparable age. At the time of the study, the patients were hospitalized for drug detoxification. Neuropsychological testing with the WAIS indicated derangement in the arithmetic and digit span subtests. PET scanning was done within 72 hours of admission to the hospital and repeated 10 days later. Subjects were drug free during this period. Seven of the 24 normal subjects showed one area of decreased CBF; of the 20 cocaine users, 14 showed at least one area of abnormal CBF before detoxification and nine after detoxification. Nine of the cocaine users showed more than one abnormal area before detoxification and six after detoxification. None of the normal subjects showed more than one abnormal area. Abnormal areas of reduced isotope uptake tend to occur more frequently in the left frontal and left parietal cortex. Cocaine abusers showed significantly lower relative CBF values for the prefrontal cortex than did the normal control subjects before and after detoxification.

Baxter et al. (115) used PET to compare cerebral glucose metabolism in an unspecified number of cocaine abusers, after 2–5 days of abstinence, to that of normal subjects and patients with unipolar and bipolar depression. Cocaine abusers did not show any changes in cerebral glucose metabolism. However, the study was limited by the number of participants and the design.

Clinical significance. A high incidence of cerebrovascular accidents following amphetamine and cocaine abuse has been reported (116, 117). The exact reasons for the deranged blood flow to the brain in cocaine abusers and its relation to the cerebrovascular disorders are unclear. There are various explanations, including activation of vasoconstrictive cerebral sympathetic fibers, vasoconstriction mediated through other neurotransmitters, cerebral vasculitis, and sudden increase in perfusion pressure (117).

Animal studies conducted with autoradiography suggest an increase in cerebral glucose metabolism in dopaminergic tracts after cocaine (similar to the increase after amphetamine). However, human studies show reduced cerebral glucose metabolism after cocaine and amphetamine. Attempts to explain these results may be premature in view of the small number of studies, the limited number of participants, and the difficulty of satisfactorily imaging most subcortical structures of interest with PET.

NICOTINE

Acute Effects

Early studies conducted with the Kety-Schmidt technique found no changes in CBF after cigarette smoking (118). Skinhoj et al. (119) measured CBF, with the xenon-133 intracarotid injection technique, and cerebral oxygen metabolism in 23 patients under resting conditions after they had smoked a cigarette. Cigarette smoking increased gray matter flow by 15.7%, and there were no regional variations. CO_2 levels did not show any appreciable changes. When cerebral metabolic rate for oxygen was computed from the difference between oxygen in blood samples from an artery and the superior jugular bulb in 13 subjects, smoking did not alter it significantly. Cerebral oxygen metabolism and CBF were measured before and after nicotine infusion (1.5 mg/mm) in 10 subjects. Nicotine increased CBF without producing any significant changes in oxygen metabolism.

Long-Term Effects

Cigarette smoking is a well-known risk factor for stroke. Kubota et al. (120), using the xenon-133 inhalation technique, found significantly lower CBF in 37 smokers after 3 hours of abstinence than in 74 matched nonsmokers. The smokers had significantly lower levels of high-density-lipoprotein cholesterol and higher total cholesterol levels, suggesting the possibility of atherosclerotic changes in cerebral blood vessels.

Rogers et al. (121) obtained CBF measurements in 268 neurologically normal subjects divided into groups of nonsmokers, smokers who had quit, and current smokers that were matched for age and sex. The nonsmokers had the highest CBF and the current smokers the lowest; the smokers who had quit were in between. CBF was also measured in 11 subjects before and after they quit smoking. CBF values increased significantly after cessation of smoking. Magnitude of increase in CBF and duration of abstinence from smoking in the first year showed a parallel relationship.

MARIJUANA

Acute Effects

We measured CBF with the xenon-133 inhalation technique in nine experienced and 17 inexperienced marijuana smokers before and after they smoked a high-potency marijuana cigarette and a placebo cigarette (122). CBF in a control group was measured twice under resting conditions. Mood states before and after smoking marijuana were quantified with the POMS. Analysis of POMS factors after marijuana smoking revealed an increase in anxiety in the inexperienced smokers and a reduction in anxiety in the experienced smokers. The inexperienced smokers also had a significant increase in depression and decrease in vigor, but neither variable changed in the other group. After marijuana, CBF decreased in the inexperienced smokers but increased in the experienced smokers, in comparison with the two measurements in the control subjects. In both groups of marijuana smokers, changes in CBF after placebo were similar to those associated with marijuana smoking. However, in the inexperienced smokers, the marijuana-induced decrease in CBF was significantly greater than that associated with placebo. There were no statistically significant differences between the increase in CBF seen after placebo and after marijuana in the experienced smokers. Anxiety, anger, fatigue, confusion, and depression had significant negative correlations with CBF, while vigor had a positive correlation. The anxiety factor was the only one to account for a significant percentage of the change in CBF (partial correlation with hemispheric CBF).

Higher anxiety levels in inexperienced smokers after marijuana smoking are well-known (123). The inverse correlation between anxiety level and CBF is in keeping with the findings reported by several other investigations (124). The increase in CBF in experienced smokers who did not become anxious after marijuana is suggestive of brain activation. The influence of the vasodilative effect of marijuana on CBF is unclear at the moment.

Long-Term Effects

Chronic marijuana smoking has been associated with a wide variety of neurobehavioral syndromes, including psychosis, mood disturbances, and confusional states (123). We measured CBF in 17 physically and mentally healthy subjects who gave histories of marijuana smoking for over 6 months and in matched control subjects (125). The marijuana smokers showed a tendency toward lower CBF values than those of the control subjects. The experienced marijuana smokers mentioned earlier (122), who were more impaired, showed lower CBF than control subjects.

Tunving et al. (126) obtained CBF measurements with the xenon-133 inhalation technique in nine chronic heavy users of marijuana who were hospitalized. These subjects were in good health except for psychiatric problems associated with cannabis use, such as sleep disturbances, anxiety, and irritability. All subjects showed high concentrations of cannabis metabolites, but no other drugs, on urine drug screens. A group of healthy volunteers matched for age and sex served as control subjects. During the first CBF measurement, hemispheric mean flow was significantly lower, with no regional differences, in the cannabis users. In four patients in whom a second measurement was made after several weeks of abstinence, the mean flow had increased by 12% and the difference was statistically significant. The flow values were adjusted for differences in CO_2 level.

Mild to moderate users of cannabis with no significant physical or psychiatric complications show normal CBF. However, heavy users of marijuana show a decrease in CBF, which tends to return to normal with abstinence. There are only two studies available on the subject, and no firm conclusions can be drawn.

INHALANTS

A wide variety of substances, including rubber cement, shoe conditioners, gasoline, ether, chloroform, and adhesives, produce a sense of intoxication when inhaled in large quantities (127–129). Large numbers of individuals, mainly adolescents and adult male homosexuals, inhale volatile nitrites for recreational purposes (130).

Acute Effects

Nitrite inhalation is followed by dilation of several vascular beds, including coronary vessels, with a decrease in systolic and diastolic blood pressure and an increase in heart rate (130). Earlier studies indicated an increase in CBF following inhalation of amyl nitrite (87).

We measured CBF, mood states, and somatic symptoms before and after inhalation of amyl nitrite in 10 physically healthy volunteers with histories of using volatile nitrites for recreational purposes (131). CBF was measured twice at a similar interval with the same technique in an equal number of normal volunteers. Inhalation of amyl nitrite was associated with a significant increase in global CBF, with no regional variation, unrelated to level of CO_2. Increase in pulse rate was the only physiological change associated with the drug. Subjects who received the drug reported a significant decrease in anger, fatigue, and depression and increased palpitation, breathing difficulty, dizziness, and headache. Changes in mood, physiological indices, and somatic symptoms after inhalation of the drug were not correlated with CBF. Amyl nitrite is a vasodilator, and this vascular effect is the most probable explanation for the increase in CBF. However, drug-induced activation of the brain might have contributed to the increase.

Most organic solvents (e.g., chloroform, ether, trichloroethylene) are vasoactive and they dilate cerebral blood vessels (74). It is unclear whether the increase in CBF is merely an epiphenomenon or is causally related to the addictive nature of these drugs. The latter would seem likely, since the inhalants that are abused are chemically heterogeneous, but all of them are cerebral vasodilators.

Long-Term Effects

Long-term exposure to organic solvents is associated with such neurotoxic symptoms as irritability, emotional lability, and memory disturbances (127–129). Most of these symptoms are reversible, indicating an underlying abnormality of brain function. House painters with a tentative diagnosis of CNS toxicity and CT findings suggestive of brain atrophy were found to have a 19% reduction in CBF, as compared to values in control subjects (132). Maximilian et al. (133), using the xenon-133 inhalation technique, showed a 6% decrease in CBF in 32 factory workers exposed to solvents. Using the same technique, Risberg and Hagstadius (134) confirmed these findings in 50 sugar refinery workers exposed to a mixture of solvents. The most marked decrease in CBF was seen in frontotemporal regions. CBF response to mental activation was preserved in these subjects. Hagstadius et al. (135) measured CBF with the same technique in 28 paint factory workers with neurotoxic symptoms while they were exposed to solvents and 24–84 months after cessation of exposure. The initial measurement showed a decrease in CBF in frontotemporal regions; this had returned to normal at the second measurement.

Clinical Significance

Cerebral vasodilation induced by these agents might account for the dizziness, syncope, and vascular headache that frequently accompany inhalant abuse (130). Rupture of a basilar artery aneurysm was reported to have accompanied sexual arousal after nitrite use in a 43-year-old man (136). The cardiovascular effects of orgasm, including tachycardia and hypertension, combined with the cerebrovascular effects of amyl nitrite may have contributed to rupture of the aneurysm. This is important, since homosexual individuals often use nitrites to enhance the orgasmic experience and to relax the anal sphincter (130). Long-term exposure to solvents is associated with a variety of neurotoxic symptoms. Reports of morphological brain changes in subjects with such exposure can be found (129). The series of studies by Hagstadius and associates show that at least some of the symptoms can be explained by brain dysfunction, as indicated by the initial decrease in CBF followed by an increase after cessation of exposure.

OTHER DRUGS

Surprisingly little information is available on the effects of opiates on CBF and cerebral metabolism. Earlier studies indicated that there was an increase in CBF after administration of morphine (74). When administered in large doses to produce narcosis, opiates reduce CBF as expected (87), except in cases where CO_2 is increased because of respiratory depression. More recently, London et al. (137) evaluated the effects on cerebral glucose metabolism of 30 mg of morphine sulfate given intramuscularly to 12 polydrug users. Morphine reduced glucose utilization by 10% in the whole brain and by about 5%–15% in telencephalic areas of the cerebellar cortex. In the absence of well-designed studies with more accurate measurement techniques, no firm conclusions are warranted. Normal subjects and schizophrenic patients given LSD did not show changes in CBF or cerebral oxygen metabolism measured with the Kety-Schmidt technique (87).

Strokes related to heroin abuse have been reported (9). A variety of mechanisms, including cerebral arteritis, endocarditis, and embolization, were implicated. Phencyclidine has been shown to lead occasionally to hypertensive encephalopathy. Cerebral vasospasm and hemiplegia after LSD injection have also been reported (9).

SUMMARY AND CONCLUSIONS

With the advent of technologically sophisticated and relatively noninvasive imaging techniques, the study of acute and long-term effects of addictive substances on CBF and cerebral metabolism has become easier. In the normal brain, CBF and cerebral metabolic rate serve as indices of brain function. This is of great importance, since in all probability, behavioral effects of drugs depend on alterations in brain function. However, drugs can induce changes in CBF through mechanisms other than brain function, such as changes in level of CO_2 (a potent cerebral vasodilator) and direct effects on cerebral vasculature.

Earlier measurement techniques, such as the Kety-Schmidt technique, were invasive, and they provided single CBF and cerebral metabolism values for the entire brain. The intracarotid injection technique, for the first time, provided information on CBF to different brain regions. The xenon-133 inhalation technique is totally noninvasive and quantitates regional CBF in both hemispheres. PET and SPECT are more recent, three-dimensional techniques that provide information on subcortical flow and metabolism.

Animal studies on the acute effects of ethyl alcohol on CBF have, by and large, yielded controversial findings. However, a series of experiments showed irreversible cerebral blood vessel spasms often followed by rupture in rat brain exposed to high concentrations of ethanol. Human studies in general indicate cerebral vasodilation; there is some suggestion that higher doses might induce cerebral vasoconstriction. The extent to which vasoactive properties of ethanol may be responsible for this is unclear. Most, but not all, studies conducted during ethanol withdrawal suggest decrease in CBF and cerebral metabolism.

Chronic alcoholism is associated with reduced CBF and cerebral metabolic rate. This reduction is partially reversible with abstinence and treatment. The effect of ethyl alcohol on CBF is particularly relevant, since it has been identified as a leading cause of stroke, especially in young adults.

Narcosis induced by sedatives and antianxiety agents leads to global reduction in CBF and cerebral metabolism. However, diazepam in nonsedating doses reduces flow to the right hemisphere, especially to the frontal lobe. Long-term treatment with clorazepate was reported to decrease glucose metabolism in the occipital and frontal cortex, especially on the right side.

Caffeine, even in small doses, is a potent cerebral vasoconstrictor. Caffeine-induced cerebral vasoconstriction (resulting from a 250-mg dose), unrelated to the behavioral and other physiological effects, lasts more than 90 minutes. Caffeine withdrawal is often accompanied by cerebral vasodilation. Caffeine's effect on CBF is relevant, since it might reduce delivery to the brain of other drugs that act on the CNS. In addition, drugs that combine caffeine and phenylpropanolamine have been reported to cause confusion, psychosis, seizures, and stroke. A decrease in CBF has been reported following ingestion of amphetamine, another commonly abused stimulant. PET scans found that cocaine abusers have abnormal CBF. Cocaine and amphetamine abuse have been associated with a high incidence of cerebrovascular accidents.

Cigarette smoke and nicotine infusion result in immediate cerebral vasodilation, presumably because of the vascular effects of the latter. Chronic smokers show global reduction in CBF, which reverses, in part, upon abstinence. Cigarette smoking is believed to be a risk factor for stroke.

Acute changes in CBF that accompany marijuana smoking seem to depend on the emotional response to the drug. Inexperienced subjects who become panicky show a decrease in CBF, while experienced subjects who become euphoric show an increase. Chronic marijuana smoking seems to induce a decrease that reverses itself with abstinence.

Most inhalants and solvents are vasodilators. Factory workers with neurotoxic symptoms related to chronic exposure to organic solvents show reduced CBF, especially in the frontotemporal regions. Removal of the person from the factory is accompanied by normalization of CBF.

Future research involving CBF and cerebral metabolism is likely to provide information of considerable clinical and research significance. The addictive properties of drugs probably depend on their ability to induce euphoria and a sense of well-being. These, in turn, depend on the increase or decrease in activity of various brain regions, which research on CBF and cerebral metabolism will help identify. Only a few studies have examined the relation between euphoria and regional CBF, and no conclusions are justified at present. Recent years have seen a surge of interest in the study of psychological and physiological characteristics of subjects who are at increased risk for alcoholism and substance abuse (138). Research on CBF and cerebral metabolism might provide information on the neurobiological correlates of such characteristics. The CNS physiology of withdrawal syndromes is another area in which this line of investigation is likely to provide useful information and might lead to the development of more effective treatment strategies. A number of addictive substances have been associated with increased risk for stroke. More information on the effects of these agents on CBF will therefore be relevant. Long-term effects of alcoholism and substance abuse involve a variety of functional and organic complications. It must be pointed out that functional and organic disorders may precede the onset of substance abuse and serve as predisposing factors. Research on CBF will facilitate the understanding of the neurobiological basis for such conditions and identify the brain regions that are affected.

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Self-Injurious Behavior: A Review of the Behavior and Biology of Self-Mutilation

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Objective: The authors describe the clinical characteristics of self-injurious behavior, giving special emphasis to self-injurious behavior occurring among individuals with character disorders. Data Collection: They review data suggesting the involvement of serotonergic, dopaminergic, and opiate neurotransmitter systems in the expression of self-injurious behavior. Findings: Self-injurious behavior occurs among mentally retarded individuals, psychotic patients, prison populations, and individuals with severe character disorders. Although theoretical psychological models of self-injurious behavior are helpful in understanding the patient's experience of self-injury, no generally useful therapeutic approach has yet evolved from these models. Data derived from animal models and treatment studies suggest the involvement of opiatergic and dopaminergic mechanisms in self-injury among the mentally retarded. Serotonergic influences on self-injurious behavior may be present in varying forms of this behavior. The scientific literature on the benefits of pharmacological agents for mentally retarded individuals is beset with a number of problems. Support is emerging, however, for the use of lithium and carbamazepine with self-injuring mentally retarded patients, and some behavioral interventions appear to be successful for mentally retarded individuals. Self-injuring patients with borderline personality disorder may benefit from milieu treatment. Conclusions: Although no form of treatment has yet been demonstrated to be of general benefit, the literature suggests that therapeutic trials with dopamine antagonists, serotonin reuptake inhibitors, and opiate antagonists may be of value.

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Self-injurious behavior is a dramatic but poorly studied phenomenon. Successful treatments of this behavior remain elusive. Among the mentally retarded, behavioral approaches have achieved some successes and occasional benefits have been described with a variety of psychotropic medications. Among other categories of self-injuring patients, such as individuals with severe character disorders, however, successful pharmacological, psychological, or psychodynamic treatment of this behavior appears to be uncommon.

In this paper we describe the clinical characteristics of self-injurious behavior. Special emphasis is given in this review to self-injurious behavior occurring among individuals with character disorders. We also review data that variously suggest the involvement of serotonergic, dopaminergic, and opiate neurotransmitter systems in the expression of this behavior. Possible models for underlying biological mechanisms may now be considered on the basis of animal models, response to treatment, and studies of neurotransmitter function in affected individuals.

We propose that self-injurious behavior be defined as the commission of deliberate harm to one's own body. The injury is done to oneself, without the aid of another person, and the injury is severe enough for tissue damage (such as scarring) to result. Acts that are committed with conscious suicidal intent or are associated with sexual arousal are excluded. Common forms of self-injurious behavior include cutting and burning the skin, banging the head and limbs, picking at wounds, and chewing fingers.

BEHAVIORAL PATTERNS

Self-injurious behavior may be categorized by the type of patient and the clinical context in which it

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occurs: 1) mentally retarded individuals, 2) psychotic patients, 3) prison populations, and 4) individuals with character disorders (primarily borderline personality disorder).

Mentally Retarded Individuals

Self-injurious behavior is a serious problem in facilities that care for the mentally retarded. Estimates of the incidence of self-injurious behavior among such patients range from 3.5% to 40% (1–3). Outward-directed aggression is also common among the mentally retarded and frequently coexists with self-injurious behavior. Although present among individuals with mental retardation of many etiologies, the most dramatic and relentless form of self-injurious behavior occurs among children with Lesch-Nyhan syndrome.

Lesch-Nyhan syndrome (4) is an X-linked enzyme deficiency disorder characterized by mental retardation, spasticity, choreoathetosis, and, often, almost unremitting self-injury. Compulsive and stereotypic self-injury, particularly finger-chewing, often requires that victims of the syndrome be maintained in almost constant physical restraints. Even in restraints, patients frequently manage to injure themselves by chewing their lips and oral tissues. Self-injurious behavior is also present among patients with another rare congenital disorder of retarded development, the Cornelia de Lange syndrome (5, 6), as well as among individuals with mental retardation of other etiologies, whose stereotypic self-injuring behavior is similar to that of children with Lesch-Nyhan syndrome and de Lange syndrome but less severe and less refractory to behavioral management. Self-injurious behavior among mentally retarded patients without Lesch-Nyhan or de Lange syndromes usually appears only after admission to a chronic care facility.

Psychotic Patients

Unlike the repetitive, stereotypic self-injurious behavior of mentally retarded patients, self-injuring acts among psychotic patients tend to be sporadic. It is among these patients that one hears of the dramatic and exotic examples of self-harm (7): autocastration, self-enucleation, autoamputation of digits and limbs, autocannibalism, and even autosurgery.

Self-injurious behavior among psychotic patients often occurs in response to command hallucinations or delusions (frequently religious in nature). Themes of punishment for guilt and sexual transgression are common (7). In one study of male patients who injured their own genitals (8), 87% were found to be psychotic at the time of the incident. Kalin (9) reported a dramatic case of a 22-year-old man who attempted to denervate his adrenal glands. The patient wanted to eliminate the production of circulating catecholamines, which he held responsible for unwanted aggressive and sexual impulses. Although his belief was based on delusional reasoning, the patient believed his behavior to be rational.

Prison Populations

There are many reports of self-injury among prisoners (10–20). Based on reports from three men's prisons, Toch (19) estimated a rate of 2.2%–7.7%.

Self-injurious behavior in prisons is difficult to assess because of poor documentation, drug use, and undiagnosed psychiatric disorders. Many self-injurious events among prisoners are suspected of being intentionally manipulative, designed to force transfer to a less restrictive facility. Isolation within prison may precipitate self-injurious behavior (12, 16, 17, 20). Virkkunen (16) compared 40 self-injuring prisoners with 40 prisoners who did not injure themselves. All (injurers and noninjurers) fulfilled criteria for antisocial personality disorder. Among the subjects who injured themselves there was a significantly higher rate of fighting, outbursts of rage, drug abuse, and anxiety.

Epidemics of self-injury have been reported in correctional institutions for teenage offenders. Ross and McKay (21) described their work with female adolescents in such a facility. In this setting, the carving of words, letters, or insignia on themselves appeared to carry consciously intended messages of group identification and assertion and may have been void of the impulsivity inherent to other forms of self-injurious behavior. However, it bears a similarity to self-injurious behavior in adult penal institutions in its seeming contagion (10), the shared forensic nature of the populations, and the facilitative effect of incarceration.

Patients With Character Disorders

Other than the notable presence of personality disorders, patients with character disorders who injure themselves do not share any single obvious trait such as incarceration, psychosis, or mental retardation.

Gardner and Cowdry (22) described the range of self-injurious behaviors they encountered in a study of self-destructive patients with borderline personality disorder. These included cuts on the wrist and the body, cigarette burns, scratching oneself with fingernails, carving words on the skin, arm- and head-banging, sandpapering the face, dripping acid on the hands, and trying to break an arm with a hammer. According to *DSM-III-R*, impulsive, self-injurious behavior—among nonpsychotic, intellectually normal individuals—may be diagnosed as either impulse control disorder not otherwise specified or as a symptom of borderline personality disorder. The anecdotal perception of an association between self-injurious behavior and borderline personality disorder developed over the past two decades.

In the 1960s, several authors (23, 24) described a category of patient called the "wrist-cutter" or "wrist-slasher." The separate grouping of these patients was largely dismissed after two studies (25, 26) demonstrated that wrist cutting did not specify a group that could be distinguished from other suicide attempters. However, the earlier studies may have been the first to suggest the presence of a group of patients, most of whom are young and female, with a high rate of self-injurious acts associated with poor tolerance of anxiety and anger.

Pattison and Kahan (27) reviewed 56 published case reports of self-injurious behavior. After excluding subjects with apparently lethal intent as well as psychotic and retarded individuals, an identifiable pattern discriminated a large portion of the reported patients. These traits include low lethality of acts, multiple self-injurious acts, and typical onset in adolescence. Pattison and Kahan did not conclude that these patients suffered from specific personality disorders and chose to refer to the "deliberate self-harm syndrome." Other authors, however, have more recently replaced the phrase "wrist-cutter" with a new designation, the "borderline self-mutilator" (28).

Self-injurious behavior by individuals in this category often bears several consistent features. Leibenluft et al. (28) described five stages of the self-injuring act: "(1) the precipitating event (such as loss of a significant relationship), (2) escalation of the dysphoria, (3) attempts to forestall the self-injury, (4) self-mutilation, and (5) the aftermath (for example, relief from tension)."

The following, quoted by Gardner and Cowdry in 1985 (22), is one patient's description: "The impulse . . . overcame the strength of my resistance not to . . . . As I started to cut, the physical pain and blood became a welcome distraction. As I cut deeper, . . . my mind began to feel relieved of the torment, my body eased of the tension, and I began to feel comforted." The development of escalating anxiety has been emphasized in the descriptions by both observers and patients (29).

The experience of pain varies among those who injure themselves. Absolute or relative analgesia for the event is commonly described (22). Leibenluft et al. (28) commented that in their experience about half of the patients who injure themselves have some degree of analgesia. Some patients report that the experience of pain is accompanied by relief. Patients' explanations for this expression of relief vary; some report feeling reassured by the capacity to feel physical sensation, assuring them they are still alive. For others it is a distraction from other dysphoric feelings, such as unbearable anger, and for others it produces a feeling of empowerment when overwhelmed by feelings of helplessness.

During the act of self-injury, many patients describe experiences of derealization and depersonalization. Such dissociated states are invoked by some psychoanalysts to explain the apparent anesthesia that allows some patients not to experience pain (30).

In 1978, Yaryura-Tobias and Neziroglu (31) suggested an association between eating disorders and self-injury. Favazza et al. (32) also postulated an association between self-injurious behavior and eating disorders on the basis of questionnaires completed by 254 subjects who said that they had injured themselves. Walsh (personal communication) reported that 27 (33%) of 81 randomly selected patients with bulimia who answered a questionnaire admitted to a history of self-injurious behavior. Jacobs and Issacs (33) compared 40 patients with anorexia with 20 normal control subjects and found that 35% of the patients with anorexia but none of the control subjects had histories of self-injurious behavior. Conclusions based on these studies are limited either by nonrandom subject selection, overinclusive criteria for self-injurious behavior, and/or dependence on the response to a single questionnaire item to identify a history of self-injurious behavior. However, in an unpublished follow-up study of 44 subjects who had been hospitalized for treatment of bulimia, Fallon and Winchel found that 39% had a history of self-injurious behavior. Data in this study were obtained by direct interview and by use of an instrument designed to assess self-injurious behavior. Just as there seems to be a high rate of histories of eating disorders among samples of individuals selected for the presence of self-injury (32), there also appears to be a high rate of self-injurious behavior among patients selected for the presence of eating disorders (33, 34).

Rates of self-injurious behavior may vary within subgroups of patients with eating disorders. Garfinkel et al. (34) observed that a history of self-injurious behavior appears to be more common among bulimic than anorectic patients. Mitchell et al. (35) found that 41% of a group of patients with bulimia who engaged in laxative abuse had a history of self-injurious behavior, compared with 26% of patients with bulimia who did not abuse laxatives. Suicide attempts were reported in a separate category in this study. Although most of these studies have methodological problems, several of them suggest that the coincidence of histories of self-injurious behavior with eating disorders ranges from 25% to 40%. The prevalence of this often hidden symptom among bulimic and anorectic patients may be underappreciated in clinical settings.

PSYCHODYNAMIC PERSPECTIVES

The psychoanalytic literature offers few theoretical treatments of self-injurious behavior. The deep human aversion to pain, however, has prompted several writers to consider two problems: what are the sources of the motivation for self-injury and by what psychological means can individuals inflict direct harm on their own bodies?

Attempting to understand individuals' motivation to wound themselves, Kafka (36) appealed to Winnicott's concept of transitional objects (37). Describing the reaction of a self-injuring patient, Kafka noted the relief experienced by the patient as she felt her own "warm" blood flowing over her skin. Kafka suggested that the blood was linked to the patient's internalized representation of her mother, which the patient sought to externalize into a soothing transitional object in times of crisis. Thus, motivation to injure oneself springs from the need to reduce intolerable feelings of tension.

Kafka suggested that it is necessary for a patient transiently to experience his or her own skin as a "not-me" object, so that the automutilation can be carried out. Pao (30) considered this problem more extensively. He hypothesized that on beginning the action of cutting, the individual enters an altered ego state. Pao compared this condition to the experience of depersonalization and derealization—the dissociated state appears to engulf some patients during the act of self-injury. The temporary suspension of ego direction allows the individual to be so directly self-damaging.

Although such considerations attempt to understand why and how individuals wound themselves, we are still left with the problem of why such an extreme measure is employed to deal with dysphoric feelings. Because of the propensity of self-injuring patients to use primitive defense mechanisms such as denial, splitting, and projective identification, psychodynamic theoreticians have tended to link such behavior to preoedipal developmental pathology. Graff and Mallin (23) have suggested that because these patients share developmental injuries in "preverbal stages," relief from tension is sought through "physical, preverbal messages." Noting frequent histories of maternal deprivation, they speculated that "the patient has protected herself against maternal rejection by introjecting her mother, allowing her to both hold onto the lost object and to deal with it by destroying that part of it within herself. . . . The pleasurable feeling derived from slashing is therefore both the joy of punishing the deprivor and a stimulatory act of self-manipulation to make up for the lack of outside stimulation."

This view of the self-injuring patient is consistent with the understanding of Grunebaum and Klerman (24). Noting the frequent use of defensive "splitting" by these patients in their relations with hospital staff, these authors stated that they "incline toward the view that the wrist-slashing patient belongs to a syndrome in the borderline group." Consequently, they recommended an inpatient treatment strategy based on ego psychology with a strong emphasis on understanding the "interpersonal dynamics of the ward social structure."

Podvoll (38), in his discussion of patients who injure themselves, also emphasized the symptom's use in relation to the community. In part, he suggested, the patient is seeking to protect himself or herself and external objects from omnivorous and engulfing demands on others. "There is a flight from deeply dependent, even symbiotic wishes toward a primitive love object to a reliance on the autoerotic use of one's own body. The symptom forestalls the more regressive strivings made upon the therapist and staff." By redirecting aggression toward oneself, "the rage and explosiveness appear to find a secure home on a fixed and seemingly indestructible object . . . and in this way the patient manages to preserve intact his split off and idealized object."

Stone (39) noted that many self-mutilating patients with borderline personality disorder have experienced sadistic sexual abuse from an older person early in life. Subsequent sexual desire, Stone suggested, is associated with extreme guilt; the self-mutilation relieves the tension arising out of guilt—the mutilation punishes not only the patient but, in effigy, the original perpetrator or perpetrators of the abuse.

Kernberg (40) recommended caution in the attribution of specific meaning to the symptom of self-injury. He questioned the pragmatic value of "metapsychological theorizing" about the meaning of self-injurious acts because of its remoteness from the patient's internal experience. He refrained from imparting any special significance to this particular symptom and cautioned the therapist against early "genetic interpretations" of the symptom. It should be noted that Kernberg did not imply that specific psychological meaning is not attributable to these acts. However, such attribution may have no practical value in psychological treatment of severe character disturbance and, indeed, may be counterproductive in early stages of therapy.

In summary, theoretical psychodynamic discussions of self-injuring individuals have been sparse. In general, such formulations have viewed these patients as having significant defects in early stages of ego development. Such deficits explain the capacity for entering dissociated states and the preponderance of other primitive defenses. The havoc they wreak on their bodies may be seen as directed toward internalized representations of others or as attempts to undo guilt. Episodes of self-injury may often be temporally linked to crises in relationships with significant others. Ego psychology provides a useful framework both for understanding these individuals and for constructing a psychodynamically based psychotherapy. However, despite the "meaningfulness" that dynamic views may contribute to attempts to understand and empathize with these individuals, no generally applicable therapeutic strategy has evolved from this framework.

BIOLOGICAL ASPECTS

The Opiate System

Painful stimulation has been demonstrated to result in increased release of endorphins (41). The presumed positive reinforcement associated with the release of endogenous opiates has been invoked as a possible explanation for repetitive behaviors that may result in opiate release. It has been suggested that the opiate system of some individuals may be altered in such a way that increased release of endogenous opiates is necessary to maintain adequate opiatergic "tone." This model has also been invoked as a potential explanation of self-injurious behavior. Opiate antagonists have been administered to patients with self-injurious behavior in an effort to diminish the theorized reward that may result from stimulation of opiate receptors. Of 25 reported patients, nine were treated with naloxone and 15 with naltrexone (42–56). One patient received both agents. Twenty-one of the patients had mental retardation of varying etiologies, three had Tourette's syndrome, and one had major depression accompanied by neurotic excoriations. Treatment and experimental methods varied widely among these reports; therefore, no conclusion regarding efficacy of these agents may be drawn. However, improvement was reported for 17 of the 25 patients. A larger, double-blind, case-controlled study of longer duration is clearly indicated.

Another indication of dysregulation of opiate systems in self-injurious behavior may come from measures of "endogenous opiates." Coid et al. (57) measured plasma neuropeptide concentrations (met-enkephalin, N-lipotropin, and β-endorphin) in patients who had been admitted to the hospital for treatment of self-injurious and other impulsive behaviors. More severely affected patients had significantly higher plasma levels of met-enkephalin. The authors noted the limitations of plasma measurements of met-enkephalin and suggested that analysis of CSF concentrations may yield more useful information.

Episodic increase in opioid activity may explain the clinical observation in many patients who injure themselves that apparent insensitivity to pain (analgesia) may accompany "dissociation" (altered alertness). As yet, there is little support for a role of opiate dysfunction associated with self-injurious behavior, but the case reports of positive effects of opiate antagonists merit further exploration.

Dopaminergic Dysregulation

Investigators have suggested that self-injurious behavior in patients with Lesch-Nyhan syndrome (5, 6, 58) and Tourette's syndrome (49, 59) may be related to dysregulation of dopaminergic activity and dopamine receptor supersensitivity. Lloyd et al. (60) have shown that CNS dopamine and its metabolites are markedly lower in patients with Lesch-Nyhan syndrome. Along with others (5, 6), Goldstein et al. (58) suggested that self-injurious behavior in Lesch-Nyhan syndrome may result from dopaminergic stimulation in a state of receptor supersensitivity.

Sokol et al. (61) reported on four patients with attention deficit disorder with hyperactivity in whom self-biting behavior was elicited by the administration of stimulants (dextroamphetamine and methylphenidate). In accord with the dopamine hypothesis of attention deficit disorder with hyperactivity, Sokol et al. speculated that these patients had dysregulation of dopamine function. They further speculated that the dopamine agonist activity of these stimulants in a supersensitive dopaminergic system resulted in self-biting, as was suggested regarding individuals with Lesch-Nyhan syndrome. However, although treatment of these patients with stimulants is known often to elicit dyskinesias and tics (also possibly linked to dopaminergic dysfunction), self-biting is not common.

Proponents of this model seek support in the observation that rats who have had chemical denervation of dopaminergic neurons with 6-hydroxydopamine exhibit self-biting behavior when administered dopamine agonists (such as L-dopa or apomorphine) (62). Goldstein et al. (63) replicated this finding. They also reported that treatment with both SCH 23390 (a selective D_1 dopamine receptor antagonist) and fluphenazine (a mixed D_1 and D_2 antagonist) blocked the elicitation of self-injurious behavior with L-dopa.

Goldstein et al. (58, 64) further investigated this model by studying monkeys who had denervation of nigrostriatal dopamine neurons. Self-biting behavior emerged in this model as well. Again, treatment with SCH 23390 (0.3 mg/kg) and fluphenazine (1.5 mg/kg) blocked this effect. However, treatment with intramuscular sulpride (100 mg/kg), a D_2 dopamine antagonist, failed to block the L-dopa-elicited emergence of self-injurious behavior. Goldstein et al. concluded that self-injurious behavior resulting from dopamine denervation and subsequent stimulation with dopamine agonists was mediated by D_1 and/or combined D_1 and D_2 receptor pathways, but not by D_2 alone. The specificity of this effect is put in doubt by the finding that rats with neonatal dopaminergic lesions also have exacerbations of self-injurious behavior when administered agonists of either the γ-aminobutyric acid (65) or adenosine neurotransmitter systems (unpublished 1988 paper of Breese et al.). In an interim report (unpublished 1988 paper), Gualtieri et al. found that fluphenazine, a predominantly D_1 antagonist, reduced self-injurious behavior in 11 of 16 mentally retarded patients.

Gillman and Sandyk (49) and Sandyk and Bamford (66) noted that the benefits of opiate antagonist administration may also be viewed in terms of the inhibitory effects of opiates on behavior mediated by the dopaminergic system. These authors suggested that if opiate antagonists do decrease self-injurious behavior, it may represent an indirect effect on the dopamine system and does not necessarily implicate opiate dysfunction in underlying pathophysiology.

Although these speculations are of interest, it should be borne in mind that the presence of dopamine supersensitivity among patients with attention deficit disorder with hyperactivity and Lesch-Nyhan syndrome is unproven. It is interesting to note, however, that self-injurious behavior is also reported among individuals with Tourette's syndrome, another condition in which speculations of hypersensitive dopamine receptors have been proposed (67) and in which dopamine antagonists have been clinically useful.

In summary, there is little evidence as yet that opiatergic or dopaminergic mechanisms are involved in the pathophysiology of self-injurious behavior. In addition, the indirect evidence that the few animal and treatment studies available yield may be relevant to understanding only self-injurious behavior associated with patients with Lesch-Nyhan syndrome and other developmental disorders. In contrast, the serotonergic influences on self-injurious behavior may be present in varying forms of self-injurious behavior.

Serotonergic System

In the light of animal data that have tied aggression to serotonergic depletion and the suggestion that self-injurious behavior represents a form of aggression, Mizuno and Yugari (68, 69) administered 1–8 mg/kg per day of 5-hydroxytryptophan, a precursor of serotonin, in an open trial to four self-injuring patients with Lesch-Nyhan syndrome. They reported a dramatic alleviation of self-injury in all four patients within 3 days of initiating medication. All patients resumed injuring themselves within 15 hours after drug treatment had stopped. This encouraging experience prompted others to administer serotonin precursors in the treatment of self-injurious behavior among children with Lesch-Nyhan syndrome.

Of seven studies published describing open-trial treatment with 5-hydroxytryptophan (68–75), two indicated improvement. The emergence of self-injurious behavior may have been prevented in another child who was treated prophylactically at an early age. Despite the indication that some modification of self-injurious behavior may occur, treatments directed at increasing serotonin availability in the CNS have not been shown reliably to diminish self-injurious behavior. In addition, self-injurious behavior may be heterogeneous, and inferences based on experience with Lesch-Nyhan syndrome may not be generalizable to other groups of patients. Regional changes in neurotransmitter function have been documented among these children compared with unimpaired children (60), further limiting extrapolation to other populations with self-injurious behavior.

Another basis for consideration of a role for the serotonergic system in self-injurious behavior is the similarity of some of its features to those of obsessive-compulsive disorder, a syndrome that has been associated with alterations of serotonergic function (76). Common to both disorders are intrusive and irresistible urges to commit an act that the individual may perceive as senseless, mounting tension associated with attempts to resist the behavior, and relief from anxiety following commission of the act. These phenomenological similarities prompt comparison between the two conditions.

Evidence for altered serotonergic function in patients with obsessive-compulsive disorder is derived from the efficacy of treatment with serotonin reuptake inhibitors (76, 77) as well as from studies of CSF concentrations of the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) (76). In addition, Hollander et al. (78) administered m-chlorophenylpiperazine, a serotonin receptor agonist, to eight patients with obsessive-compulsive disorder. Six demonstrated a significant exacerbation of symptoms.

Several authors (31, 79) have reported that symptoms of self-injurious behavior in patients with coexisting obsessive-compulsive disorder responded to treatment with serotonin-reuptake inhibitors. Trichotillomania (hair-pulling) and nail-biting may represent variant forms of self-injurious behavior. In pilot trials (80, 81) these conditions have been reported to respond to fluoxetine and clomipramine. Patel et al. (82) described successful treatment of self-injurious behavior with trazodone in a patient with recurrent major depression. The medication was stopped and restarted several times for clinical reasons. Self-injurious behavior was alleviated each time medication was instituted and returned on each discontinuation. There was no concurrent improvement in depression.

Using neuroendocrine challenge tests as measures of serotonergic activity, Coccaro et al. (83, 84) studied patients with various personality disorders and observed that the *DSM-III* borderline personality disorder item "self-damaging acts" was associated with the greatest variance from control subjects (84).

5-HIAA is the major metabolite of serotonin, and its concentration in the CSF has been demonstrated to be a reliable index of serotonin concentration in the brain (85). Lopez-Ibor et al. (86) measured CSF 5-HIAA and rated the presence of "self-injuries that do not constitute a vital threat" in 21 patients with major depression. Five of the 21 patients exhibited self-aggressive behaviors. These five patients had significantly lower CSF 5-HIAA concentrations than the remaining 16 patients.

Investigations of the significance of serotonergic activity in self-injury were prompted by observations of serotonergically mediated effects on aggression in laboratory animals. In 1967, Valzelli (87) observed that various monoamine oxidase inhibitors (MAOIs), such as pargyline, increase brain serotonin more slowly in aggressive rats than in normal rats, suggesting some alteration of serotonergic turnover. He also demonstrated that administration of other serotonergic agents can induce aggressive behavior in laboratory animals. Shock-induced fighting can be potentiated by pretreatment with 5,7-dihydroxytryptamine, which depletes serotonin (88). P-Chlorophenylalanine, an inhibitor of serotonin synthesis, increases aggressive (89) and filicidal (90) behavior in rats. Mouse-killing (muricidal) behavior in rats may be induced by electrolytic (91) or neurochemical (92) lesions of serotonergic nuclei. Aggressive behavior that follows mechanical lesions of the olfactory bulb may be reversed by subsequent treatment with 5-hydroxytryptophan (89). Muricidal behavior in isolated rats was inhibited by administration of L-tryptophan, a precursor of 5-hydroxytryptophan (93).

Manipulations of other neurotransmitter systems, however, such as dopaminergic (94) and adrenergic (88) systems, have also demonstrated modulatory effects on aggression in rats. In addition, there are various forms of animal aggression that may have distinct neurochemical correlates. Further complicating extrapolation, different species may vary in response to neurochemical manipulations (95). Nevertheless, these findings provided the basis for initial speculation that self-injurious behavior may be associated with altered serotonergic function.

Although neurochemical examinations of self-injurious behavior have focused on dopamine, opiate, and serotonin systems, Kopin (96) suggested that the diazepam-binding site may be implicated. His speculation was based on the observation that caffeine, a methylpurine derivative that can elicit self-injurious behavior in laboratory animals, inhibits the binding of diazepam to its receptors. The accumulation of oxypurines in the brains of children with Lesch-Nyhan syndrome lends circumstantial support to this suggestion.

TREATMENT

Pharmacological

The scientific literature on the benefits of pharmacological agents in the treatment of self-injurious behavior is made up mainly of studies of mentally retarded persons. Several extensive reviews of this literature have been published (3, 97–100), and it will not be detailed here. Agents that have been examined include neuroleptics, lithium, carbamazepine, minor tranquilizers, propranolol, baclofen, stimulants, and antidepressants.

The reports are beset with a number of problems. Their methods differed greatly. No standard and/or reliable scale of self-injurious behavior has been developed. The need to intervene to stop self-injury may hide partial benefits. Patients with mental retardation of disparate causes were grouped together in some studies, and in some reports no distinction was made between self- and outward-directed aggression. Nonspecific sedating effects (as with neuroleptics and benzodiazepines) or the presence of undiagnosed mood disorders (which may respond to lithium and carbamazepine) complicate the interpretation of beneficial effects. The frequent presence of seizure disorders or nonspecific EEG abnormalities in this population further obscures the putative benefits of carbamazepine. Although neuroleptics are extensively used in attempts to control self-injurious behavior, it is not clear that there is sufficient benefit to justify the exposure to the morbid side effects of these drugs.

Despite the tentative nature of the available data, considerable support is emerging for the use of lithium and carbamazepine with mentally retarded patients who injure themselves. Lapierre and Reesal (99) urged caution in the use of lithium, noting that organic brain pathology in these patients may predispose them to toxic side effects. The use of serotonergic agents has already been reviewed here. None of these approaches has yet yielded persuasive evidence of general efficacy.

There are no systematic treatment studies of self-injurious behavior in other self-injuring populations (psychotic patients, prisoners, and patients with character disorders). Among psychotic patients, whose self-harm tends to be episodic and unpredictable, usual modes of treatment for the overall illness—as well as measures taken to prevent imminent self-harm—would seem to be prudent.

Studies of pharmacological treatment for patients with character disorders may offer some guidelines for treatment of self-injurious behavior. Liebowitz (101) emphasized the interpersonal losses that often appear to precede bouts of self-injurious behavior among such individuals. He and Klein (102) compared this phenomenon to the "rejection sensitivity" noted in patients with the "hysteroid dysphoric" form of atypical depression. Liebowitz et al. (103) stated that treatment of depression with MAOI antidepressants among such individuals may be superior to treatment with tricyclic antidepressants. Cowdry and Gardner's study of the treatment of patients with borderline personality disorder (104) supports the notion that the MAOI tranylcypromine is specifically useful for the rejection sensitivity of these patients. Extrapolating from this experience, Liebowitz (101) suggested consideration of MAOI medications for treatment of self-injuring patients.

Cowdry and Gardner (104–106) compared the benefits of tranylcypromine, alprazolam, carbamazepine, trifluoperazine, and placebo in patients with borderline personality disorder. Their findings in relation to tranylcypromine and rejection sensitivity (104) have already been noted. They also examined the effects of these medications on episodes of impulse dyscontrol (including self-injuring behavior). Although the neuroleptic and the MAOI showed trends toward fewer episodes of such behavior, only treatment with carbamazepine demonstrated a significant decrease in the number of such episodes. Alprazolam trials resulted in a significantly greater rate of severe dyscontrol than did placebo trials.

As already noted in this paper, self-injurious behavior and obsessive-compulsive disorder may share important clinical features. The successful introduction of serotonin reuptake blockers for the treatment of obsessive-compulsive disorder may indicate that trials of such medications for self-injurious behavior are warranted.

Behavioral

A large body of literature has examined the environmental contingencies in which self-injurious behavior occurs among mentally retarded persons. Many attempts have been made using a variety of conditioning techniques to diminish self-injurious behavior. As summarized by Carr and Durand (107), "factors responsible for the maintenance of behavior problems fall into two broad classes: escape behavior, controlled by negative reinforcement processes, and attention-seeking behavior, controlled by positive reinforcement processes." An example of the former may occur when classroom demands are experienced as aversive. Self-injuring behavior would be likely to result in removal from the demand situation. In an example of the latter, verbally impaired children may find that they can elicit adult attention by injuring themselves. This observation has resulted in attempts to reduce self-injurious behavior by teaching communication skills (107). Durand and Crimmins (108) reported on the use of an instrument designed to identify the variables that maintain self-injurious behavior.

Other behavioral techniques that have been used include extinction, sensory extinction, punishment, alternative-sensory activities, timeouts, and overcorrection (109). Some of the methodological problems that have been discussed in regard to pharmacological trials apply to these trials as well, particularly the need to intervene to reduce injury and the lack of standard, reliable rating instruments. Behavioral treatment methods are labor-intensive and, despite their apparent potential for diminishing self-injurious behavior, may be extremely difficult to implement on a large scale. Nevertheless, some behavioral interventions appear to be successful, and they present none of the risks associated with pharmacological approaches.

Milieu Therapy

Inpatient units with treatment environments dedicated to the identification and containment of acting-out behaviors have been advocated for the treatment of patients with borderline personality disorder (110). In such environments, patients' attempts at "splitting" staff and uses of other primitive forms of psychological defense are readily identifiable and made accessible to interpretation. Self-injuring patients with borderline personality disorder may benefit from such treatment. Similarly, Grunebaum and Klerman (24) supported an inpatient treatment strategy based on ego psychology with a strong emphasis on understanding the "interpersonal dynamics of the ward social structure." It may be particularly important in such an environment carefully to guard against surreptitious self-harm. The milieu's challenge to the patient's defensive structure may motivate the use of defenses that may be kept "invisible" from staff.

Another approach is taken in an inpatient program directed to the treatment of self-injurious behavior (111). Patients are admitted for 30 days; on admission they sign a no-harm contract in which they commit themselves to refrain from self-injury and to approach a staff member should the inclination arise. A single episode may result in discharge from the program. During their hospital stay, patients are discouraged from focusing on self-injurious behavior and are urged to examine other stresses in their life, such as deteriorating marriages or histories of incestuous assault.

Since these approaches depend on labor-intensive and costly inpatient treatment, demonstration of efficacy is important. Both approaches are grounded in clinical experience, but no systematically obtained data are available concerning either short-term or long-term benefits to patients in the reduction of self-injurious behavior.

Self-Help Groups

Several self-help groups exist in different U.S. cities for patients with self-injurious behavior. Some have modeled themselves after the 12-step program of Alcoholics Anonymous. The courses of individuals who participate in these programs have not yet been examined.

DISCUSSION

Confinement, Serotonin, and Isolation

Confinement may be a specific provocateur of self-injurious behavior for vulnerable persons. The contexts in which self-injurious behavior occurs include prisons (10, 12), corrective institutions for adolescent offenders (21), inpatient facilities for the mentally retarded (1–3), and inpatient adolescent psychiatric units (112). In each of these contexts, some individuals are described who have no history of self-injurious behavior until admission.

If certain personality disorders predispose an individual to self-injurious behavior, the apparent prevalence of self-injurious behavior in prisons may be a consequence of the presence of such pathology among inmates. Within this high-risk population, certain characteristics may be associated with greater vulnerability to self-injurious behavior. Virkkunen (16) found a higher rate of impulsivity and antisocial traits among self-injuring prisoners than among non-self-injuring prisoners.

The observation that imprisonment may elicit self-injurious behavior in humans prompts comparison with self-injury among animals. Jones (29) observed that "practically all known reports of self-injury in macaques [a primate] have been recorded when the animal is physically restricted and usually when isolated." Although comparisons between human behavior and animal behavior should be made cautiously, the similarity in potentiating conditions for self-injury is of interest—and may even reflect an ethological basis for the "aloneness" that seems to precipitate self-injurious behavior among individuals with borderline personality.

Isolation has long been known to increase aggression in rodents (87). Valzelli and Bernasconi (113) studied seven strains of mice who had been housed in either grouped or isolated conditions. Severity of isolation-induced aggression was scored and brain 5-HIAA concentrations were subsequently measured. Those strains in which brain 5-HIAA differed between isolated and nonisolated conditions also demonstrated the highest aggression scores. This study suggests that isolation may be associated with decrements in serotonin turnover in certain strains of mice and that this decrement may be associated with isolation-induced aggression. It is tempting to consider that conditions which are apparently associated with increased self-injurious behavior in humans (such as solitary confinement and object loss) may bear similarities to the isolation of laboratory mice.

The Search for Biological Markers

Recent years have seen the emergence of a symptom-based approach to the study of biological bases of psychopathology. Narrowing the focus of CSF neurochemical studies from depressive syndromes to suicidal behavior (114) revealed an association between altered serotonergic function and suicidality, an association that crosses traditional diagnostic lines. Other studies that narrowed the search for markers from syndromes to individual symptoms have yielded new findings associating impulsiveness—in particular violent impulsive behavior—with markers of altered serotonergic function (83, 115). Similarly, it is reasonable to consider that self-injurious behavior in various conditions may have a common organic component, independent of coexisting syndromal diagnoses.

This notion is of great clinical significance because it suggests the potential for independently treating individual morbid symptoms in the context of overall refractory conditions such as schizophrenia and severe depression. As we have discussed elsewhere (114), although individuals afflicted with refractory illnesses may have other symptoms, specific relief from suicidal impulses, for example, may be of great benefit. The relief of specific symptoms may be of great pragmatic value for patients who suffer from self-injurious behavior in the presence of intractable conditions, such as mental retardation and severe personality disorder.

CONCLUSIONS

We have reviewed data suggesting that self-injurious behavior may be associated with serotonergic dysfunction. Although the evidence is not conclusive, it does prompt speculation regarding variant symptoms that appear to be related to alterations of serotonergic function. In particular, suicidal behavior (114), obsessive-compulsive disorder (76), fire-setting (115), and impulsive violence (115) have been shown to be associated with changes in various serotonergic measures. If these symptoms are, indeed, the sequelae of serotonergic dysfunction, they may be the result of varying physiological lesions. Alternatively, all or several of these symptoms may represent variant expressions of a common lesion. In addition to its theoretical significance, this question has important implications for the conduct of psychiatric research, particularly familial and genetic research. Studies that are dependent on identifying affected individuals must be able to identify variant expressions of physiological defects.

Although the data to support such a conclusion are still inadequate, it is reasonable to speculate that a cluster of symptoms is emerging which share both altered serotonergic function and elements of impulse dyscontrol. Given the complexity of neurochemical interactions, it is likely that more than one neurotransmitter system will be ultimately implicated in these behaviors. Nevertheless, these converging observations strongly suggest the value of examining serotonergic function as it may mediate impulsiveness. The developing repertoire of techniques that are becoming available for clinical study of this system makes it a functionally useful starting point.

We have reviewed the scientific literature regarding self-injurious behavior. Two issues raised by other authors should be mentioned.

Several authors (39, 116) have observed frequent histories of childhood sexual assault among individuals with self-injurious behavior, and some have concluded that self-injurious behavior in these individuals may be the outcome of such abuse. In an unpublished survey of bulimic patients, Fallon and Winchel found that such abuse was more frequently reported among patients who injured themselves but that not all patients who injured themselves reported histories of abuse. Although the importance and grave traumatic effects of childhood sexual abuse should not be underestimated, a cause and effect relationship between abuse and self-injurious behavior should not be automatically assumed. Sexual abuse may serve to elicit symptoms in an individual already at risk, but frequent histories of such trauma may also reflect a familial predisposition to impulsive—and perhaps violent—behaviors. An interplay of both factors suggests the unfortunate possibility that those who are biologically endowed with a vulnerability to self-injurious behavior may also have a greater probability of being raised in a familial environment where the stresses that might elicit such behavior—such as childhood sexual abuse—are more likely to occur.

Another issue that has been raised has been the suggestion that a triad of symptoms (self-injury, eating disorder, and alcohol abuse) deserves a separate diagnosis in *DSM-IV* (27). In our experience, a substantial number of patients with this triad may be identified. It is not yet clear, however, that a separate designation would specify anything other than a subgroup of existing categories, such as borderline personality disorder. If an individual with self-injurious behavior does not otherwise meet criteria for borderline personality disorder or antisocial personality disorder, the *DSM-III-R* diagnosis of impulse control disorder not otherwise specified may be applied to these patients. The frequency of this proposed triad among individuals with self-injurious behavior deserves investigation.

In summary, self-injurious behavior is a poorly understood phenomenon in both its behavioral and biochemical aspects. It occurs in a variety of clinical settings, and features of the behavior vary among these settings. Isolation, confinement, and interpersonal traumata may facilitate the expression of these behaviors. Mental retardation, criminal sociopathy, eating disorders, and borderline personality may be associated with self-injurious behavior. We have reviewed data suggesting that serotonergically, opiatergically, and/or dopaminergically mediated processes may be implicated in self-injurious behavior. Although no form of treatment has yet been demonstrated to be of general benefit, these data suggest that therapeutic trials with dopamine antagonists, serotonin reuptake inhibitors, and opiate antagonists may be of value.

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A Psychodynamic Perspective on the Clinical Impact of Insurance Review

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The rise of managed care and concurrent utilization review has had a profound impact on the practice of inpatient psychiatry. Little has been written, however, on the clinical impact of the review process itself. The actions of insurance reviewers often result in their being incorporated into the psychopathology of individual patients and into the dynamics of families and institutional settings. The authors apply psychodynamic understanding to a series of case examples to illustrate how concurrent review may promote splitting, impede the patient's ability to separate from the hospital, and paradoxically reinforce the patient's illness. They also explore a number of typical responses of treatment staff and families to the review process. A case vignette demonstrating a sincere effort at mutual collaboration between payers and providers is also presented. This spirit of compromise is proposed as the solution that best serves patient care.

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In recent years, psychiatrists who work in inpatient settings have borne witness to an unprecedented scrutiny of third-party reimbursement. Concurrent utilization review, managed care, and preadmission certification programs have profoundly affected the autonomy of psychiatrists involved in hospital treatment to the point where many practitioners are feeling that treatment is no longer under their control. Sargent (1) has noted, "A harsh, inflexible scrutiny best called 'relentless review' . . . threatens to dominate the field . . . . Psychiatrists, like other physicians, often are caught between a professional duty to assert a patient's need for continued care and a faceless utilization reviewer who declares that further treatment is not covered because it is not 'medically necessary.' " These influences, in addition to such changes in the delivery of health care as health maintenance organizations and preferred provider organizations, have contributed to a dramatic decrease in the length of stay for psychiatric inpatients. In fact, over the last 30 years the average length of stay has fallen by more than two-thirds (2).

Insurance reviewers come in varied forms: they may be employees of the insurance company, independent consultants (often psychiatrists) contracted by the company, or employees of a managed-care firm retained by the insurance company. The current trend seems to be in the direction of the lattermost variant—approximately 70% of employees are now under a managed-care arrangement (3). These managed-care firms have come to be known as "fourth parties."

Regardless of the type of review involved, clinicians treating inpatients have experienced a substantial erosion of the time they have available for providing treatment (2, 4). Time formerly devoted to clinical purposes has been appropriated by extensive requirements for documentation, weekly (or evenly daily) phone calls with reviewers, and letters to justify continued hospitalization. The cost of all these additional duties is, of course, absorbed by the hospitals.

As problematic as these sweeping changes in the mental health care scene may be for psychiatrists, their

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impact on patients is of far greater concern. As Melnick and Lyter (4) observed, "Getting patients out may become more important than getting patients well." Decisions regarding mental health care delivery are characteristically made at the administrative level, and patients' needs are given the least consideration (5). Clinicians are plagued with uncertainty regarding the length of stay they will be allowed for a given patient. Treatment planning becomes chaotic in a climate where one does not know from day to day whether the coverage will be continued.

The clinical impact of insurance review is particularly important for a subgroup of treatment-refractory patients who do not respond to outpatient psychotherapy, pharmacotherapy, or brief hospitalizations. The size of this group has been estimated to be 10%–30% of the clinical population seen in hospital settings (6). Insurance companies have become particularly reluctant to reimburse treatment for these patients because they require more extended hospitalizations. Part of this resistance may relate to the historical stigmatization of patients with severe mental illness (7). In addition, many reviewers view their primary mission as cost containment.

Reports are now appearing that reflect the adverse impact of premature discharge on patients from this subgroup (2, 8). Patients with recurrent impulsive behavior of a life-threatening nature often need a highly structured environment to prevent intentional or accidental suicides. These difficult-to-treat patients and the clinicians treating them often feel in a bind, which Sharfstein et al. (6) have aptly termed a Catch 22 situation: If the patient shows signs of improvement, the insurance reviewer may insist on discharge; if the patient is making no progress, the reviewer may still insist on discharge on the basis of the premise that the treatment is merely custodial.

Little has been written on the psychodynamic aspects of insurance reimbursement. The literature that does exist (9–12) has derived from the setting of outpatient psychoanalysis. Thus far, to our knowledge, no one has applied psychodynamic understanding to the clinical impact of insurance review on patients, families, and clinicians. The following case examples illustrate how the insurance review process itself may be incorporated into the psychopathology of individual inpatients and into the dynamics of families and institutional settings.

IMPACT ON PATIENTS

Case 1. Mr. A, a 34-year-old man, was admitted to a psychiatric hospital for problems of depression, recurrent suicidal feelings, and difficulty controlling his temper outbursts. His diagnoses were borderline personality disorder and major depression. A psychiatric consultant hired by Mr. A's insurance company called the attending psychiatrist several days after the patient's admission and asked how he was doing. He interrupted the psychiatrist in mid-sentence and asked sarcastically, "Do you *really* think you can do anything for this patient?" Before the psychiatrist could answer the question, the reviewer asked about antidepressant medication. Mr. A's psychiatrist explained that he was ascertaining Mr. A's imipramine level and would consider switching to phenelzine if Mr. A continued to be unresponsive to a therapeutic level of imipramine. The reviewer told Mr. A's psychiatrist that he preferred tranylcypromine over phenelzine and suggested that the switch should occur immediately.

Mr. A's psychiatrist experienced the reviewer as rude, intrusive, and attempting to control the treatment. He got the impression that if he did not follow the reviewer's suggestions, the patient's stay would not be recertified. Mr. A was told about the reviewer's pressure to get the treatment over with as quickly as possible; he then began to regard the reviewer as a villain who was working against the treatment team. Anger that might have been directed at the treatment team was instead displaced toward the reviewer, who, to a large extent, was an easy target because of his behavior. Meanwhile, Mr. A idealized his physician as a rescuer—a white knight leading the charge against an unreasonable and intrusive monster.

Many of the patients who require extended hospital treatment suffer from borderline personality disorder (13–16). Splitting, of course, is the principal defensive operation found in borderline patients (17, 18) and often manifests itself in the division of the hospital treatment staff into camps of "good objects" and "bad objects" (15, 19, 20). Bad object projections are not randomly assigned (19–22). An insurance reviewer who is particularly hostile or adversarial may serve as an ideal nidus for the projection of the bad internal object representation. In such cases the reviewer's behavior, as well as the psychiatrist's response to it, may actually promote and intensify the patient's preexisting propensity to employ splitting.

When the insurance reviewer serves as a repository for the patient's bad object projections, it may lead to a major complication in the patient's attempt to separate from the hospital and engage in a psychologically meaningful discharge process.

Case 2. Ms. B was a 20-year-old college student who remained suicidal despite a series of intermittent brief hospitalizations and outpatient treatment over a 3-year period. Her diagnosis was borderline personality disorder, and her admission to a psychiatric hospital for extended treatment was precipitated by a suicide attempt. Following the patient's admission, a case reviewer began calling Ms. B's physician on a weekly basis to find out if the patient truly needed to be in the hospital.

Nine months after her admission, Ms. B was making steady improvement and had formed substantial attachments to the treaters. The case reviewer began to demand a discharge date for the patient. Ms. B's psychiatrist explained to the case reviewer that the patient was still seriously suicidal and that the treatment team had to help the patient gradually separate from the important treatment relationships she had formed in the hospital. The case reviewer insisted on a discharge date and finally indicated that she wanted to talk to Ms. B directly. Ms. B, on learning of this request, became increasingly fearful of the reviewer and the possibility that her treatment would be abruptly terminated. In group meetings on the unit Ms. B repeatedly referred to her fear that she would be "kicked out" by her insurance company before she was ready. She was preoccupied with this concern and became increasingly suicidal as she contemplated the threat of premature discharge.

Ms. B's reaction to this perceived external threat from the case reviewer was to attach herself more intensely to the treatment team. This reaction made it even more difficult for the patient to separate from her treaters in a meaningful way. When the case reviewer forced the patient out of the hospital, she promptly attempted suicide several days after her discharge and had to be rehospitalized.

Empirical research has demonstrated that careful discharge planning is essential to assure treatment compliance and avoid rehospitalization (23). One reason that the discharge process is important in extended hospitalization is that patients must be able to disengage gradually from the meaningful relationships they have formed in the hospital and develop new attachments. Instrumental to this mourning process is coming to terms with both the "good" and the "bad" aspects of the treaters. Indeed, one major goal in the treatment of borderline patients is the integration of the split-off fragments of self-representations and object representations into more mature, ambivalent views (18). Ms. B was unable to accomplish this integrative task because all "badness" was perceived as residing in the threatening insurance reviewer. Moreover, she became more attached to the staff members of her treatment team in an effort to protect herself from the threat of external attack.

The case of Ms. B also illustrates how the close scrutiny of the insurance company may in and of itself become a major stressor to the patient. In fact, in some cases hospital psychiatrists have found it necessary to include the insurance review process as a new problem on the patient's problem list in the medical record. This scrutiny itself may create an atmosphere in which patients feel they cannot improve without disastrous consequences. In so doing, the insurance review may have the paradoxical effect of reinforcing the patient's illness. Patients may feel that they must stay suicidal in order to avoid losing their entire support system of treaters.

IMPACT ON TREATERS

Inpatient treatment staff may respond to review by insurance companies in much the same manner as patients. Although they may be better able to handle the stress of the review because of greater psychological resources, they nevertheless are influenced in such a way that their treatment skills may be seriously compromised. It is often highly tempting for the treatment team to collude with the patient in the projection of all badness onto the insurance reviewer. Primitive defensive operations such as splitting and projection are also common in staff groups, and staff members may readily fall into a pattern of seeing the reviewer as the container of all badness in the treatment system (20). (A similar risk exists with family members, who may be seen as the villains who caused the patient's illness.) Being the target of the borderline patient's hatred and contempt is exceedingly unpleasant, and there may be a sense of relief in having it directed elsewhere, especially at a figure whom the treatment team already regards with considerable hostility. With patients who are extraordinarily hateful and seem to be incapable of forming a therapeutic alliance, it may be particularly attractive to forge an alliance through siding with the patient against a common outside enemy (14, 15). However, this temporary solution is doomed to failure because the alliance rests on an unstable foundation—namely, the splitting and projection of all negative feelings between the patient and the treatment team. It is only a matter of time until the tables are turned and the treaters are once again regarded as the patient's bad objects. This turn of events may explain the fact that a dissatisfied patient often chooses to sue the physician rather than the insurance company (1).

Treatment staff may also feel cornered into a situation of demanding improvement at a rate with which the patient cannot reasonably comply. This pressure creates a situation that Rinsley (24) termed "depersonification." The fact that the patient may be developmentally arrested at a psychological age of 18–24 months is disregarded, and staff members expect the patient to behave as a mature adult would. Patients in these instances feel terribly misunderstood and experience these expectations as totally beyond reach. As a result, patients experience a severe blow to their self-esteem and deteriorate further. Depersonification of this nature is often a repetition of what these patients experienced at home, where they may have been regarded as bad instead of psychologically disturbed. Even in the best scenario, these patients may be able to provide only a kind of "false self" compliance—they marshal their ego resources to comply with expectations, but no internal change has occurred beneath the surface.

Case 3. Ms. C was a 26-year-old patient with a diagnosis of schizoaffective disorder and severe suicidal tendencies. She had a 7-year history of recurrent psychotic episodes and suicide attempts. She was admitted to an extended-treatment unit of a psychiatric hospital after numerous failures of short-term hospitalizations and pharmacotherapy. While a teenager, she was constantly compared with an older sister who was the "star" of the family. Her parents repeatedly told her that she was "nothing but trouble." As her psychotic symptoms evolved, she would tell her parents, "I think I'm crazy," only to have them respond that she was bad and needed discipline rather than treatment. Her parents finally made her leave the house because she would not behave. When she tried to return home, her parents called the police.

Following Ms. C's admission, a managed-care firm hired by her insurance company immediately made it clear that they expected rapid results. Although the patient was admitted for extended treatment, they would approve only a month at a time, always with the expectation that the patient ought to be out of the hospital by the end of the month. The patient experienced this expectation as a repetition of her mother's demands that she behave—with the threat of being kicked out of the house if she did not. She said that she would kill herself if she had to leave prematurely.

The staff members on the treatment team were acutely aware of the severity of Ms. C's psychiatric disorder. When the insurance company threatened discharge, the team's anxiety level skyrocketed. They were extremely worried that the patient would kill herself if she were discharged prematurely, and they conveyed a "hurry-up-and-change" attitude to Ms. C, who felt unable to improve at the rate they expected. The pressure from the managed-care firm reviewing the case led to a situation in which the treatment team was much more invested in the patient's improvement than she was. Suffering had become a way of life for the patient, and she was unable to rapidly change her habitual mode of relatedness. High expectations of staff members had the paradoxical effect of leading to further deterioration. Ms. C experienced these expectations as a recapitulation of her family situation, where the expectations of change exceeded her level of psychological development. She felt that staff members were not empathizing with her difficulties or understanding her limitations. In other words, she felt depersonified.

For treatment-resistant patients who require extended hospitalization, change is often a dirty word. Besides the humiliation of feeling unable to meet the standards set by treaters, demands for improvement often convey the message that patients are unacceptable as they are and must be different to be acceptable. Numerous authors (15, 25, 26) have cautioned against excessive zeal in the treatment of borderline patients. In response to the feeling of being misunderstood and humiliated, many patients will dig in their heels and become more oppositional. There is often an unconscious feeling of triumph at defeating the treater who is consumed with a *furor therapeuticus*. This delight in thwarting the treater's efforts will increase in direct proportion to the treater's investment in changing the patient. Psychodynamic exploration of such cases often reveals deep-seated revenge fantasies against one's parents (27).

Among the subgroup of borderline patients who seem to require prolonged hospitalization, a fair number suffer from organically based cognitive deficits (28–31). The key to successful treatment of these patients is often accurate diagnosis and reduced expectations of performance by both family and treaters. Paradoxically, these patients often improve more when the pressure to change is removed (30, 32).

Insurance reviewers often have an alarming lack of interest in dynamic factors such as these in the patient's failure to improve. Some observers (4) have suggested that evidence of improvement in the patient is not a valid review criterion. As these examples demonstrate, this criterion may create an atmosphere that subverts treatment.

IMPACT ON FAMILIES

The hospitalization of an adolescent or young adult may pose a serious threat to the family equilibrium. Especially in families where enmeshment is a major dynamic, the hospital treatment may be viewed as an effort to undermine the family relationships and make the patient become autonomous from the family (32, 33). In these instances parents may harbor a deep sense of mistrust toward the treatment team and may be skeptical about their competence or intentions. When an insurance company conveys some doubt about the validity or efficacy of the hospital treatment being delivered, such families may pounce on this skeptical attitude as confirmation of their own doubts. The result is an "unholy alliance" between the family and the insurance company.

Case 4. Mr. D was an 18-year-old patient who had numerous run-ins with law enforcement agencies as a result of antisocial behaviors, such as driving while intoxicated, writing bad checks, and stealing. When the patient became depressed and suicidal, he was admitted to a psychiatric hospital. Mr. D's widowed mother felt that her life revolved around her son and was wary of what might transpire during the hospitalization.

After 3 months of hospitalization, Mr. D continued to be intensely suicidal. His mother asked the social worker on the treatment team why her son could not come home. She questioned whether he was truly suicidal and volunteered to watch him herself to prevent him from doing anything. About this same time, the insurance company contacted Mr. D's mother and told her that they questioned whether continued inpatient treatment was advisable. Seizing on this information as a validation of her own skepticism, she called the social worker and argued again for her son's discharge. This time, however, she bolstered her argument with key words she had learned from the insurance company. For example, she said that suicide was only a "potential," not an "imminent," threat. She argued that suicide was a potential for most people, and she suggested that the treatment team might simply be using it as a ruse to assure continued coverage. She made a point of saying that since the insurance company agreed with her point of view, there must be some legitimacy to it.

This form of collusion between insurance companies and family members may cause the treatment team and the patient to "circle the wagons" against the outside intruders. On the other hand, patients who are opposed to staying in the hospital may ally themselves with the insurance reviewer against parents and treaters to force a discharge that is highly premature. Adolescent patients frequently view the case reviewer as a savior or fairy godmother who will rescue them from the hospital (personal communication from H.J. Green).

An opposite situation that is also common is the development of an alliance between the treatment team and the family against the insurance company. In many cases the insurance company has contractually agreed to a much higher level of benefits than they are actually willing to contribute to an extended hospitalization. The family members involved may be forced to file a lawsuit against the insurance company to get the coverage that they have been guaranteed. (In describing this development, we do not mean to imply that the necessity of suing the insurance company for benefits is a pathological event. Families may be forced into this situation when they are denied benefits they have been promised.)

INSURANCE REVIEW AS COLLABORATION

Case reviewers should have two roles: that of patient advocate and that of container of costs. These two functions must always be balanced against one another with the awareness that what is best for the patient may not always be the cheapest solution (34). Moreover, one extended hospitalization early in the course of an illness may be more cost effective in the long run than a series of many brief hospitalizations spread out over decades.

Insurance reviewers who have the best interests of the patient in mind consider themselves collaborators with the treatment team. They do not portray themselves as perfect individuals who provide a never-ending flow of money in an unlimited manner, but they work with the treatment staff toward a compromise that attempts to balance cost containment with what is clinically indicated for the patient.

Case 5. Ms. E was a 33-year-old single woman with a refractory depression. Every major antidepressant medication had been tried in her treatment, and she had had three separate courses of ECT. She had made several serious suicide attempts and had a serious alcohol problem as well. After 27 brief hospitalizations, her case reviewer referred her to a psychiatric hospital that specialized in extended treatment. Based on the failure of her previous short-term hospitalizations, the reviewer readily accepted the need for more extended hospitalization. She asked to be kept informed of the patient's progress, and she offered to attend a case conference set for approximately 2 months after admission. She attended the conference and listened intently to the discussion about Ms. E, the dynamic understanding of her illness, and the treatment plan that was necessary to make a substantial impact on her illness. The case reviewer authorized continued treatment for 6 months so that the plan would have a fair trial.

After 6 months, the reviewer asked if the patient could be moved to a less expensive setting such as a day hospital. The treatment team felt that the patient had improved sufficiently to give such a plan a try. The case reviewer recognized that an abrupt transition would cause the patient to lose the gains she had made during the hospital phase of treatment, so she collaborated with the team in planning a 2-month transition. This enabled the patient to gradually disengage from her relationships with the treatment team and form new relationships with the staff members in her partial hospitalization program.

DISCUSSION

In an age of increased international competition and escalating health costs, it is understandable that industry is increasingly turning to managed-care firms for help in controlling the costs of insuring their employees. Unfortunately, the impact of the scrutiny of health care costs on employees has often been neglected in the planning and implementation of these cost-saving measures.

Abuses by hospitals have undoubtedly occurred, and some scrutiny of the provision of services is necessary. However, the psychodynamic considerations discussed in this paper underscore the fact that the more adversarial and irrational the review process becomes, the more likely it is to feed into the patients' and the families' preexisting psychopathology and thereby undermine or compromise the treatment. A key feature of extended hospital treatment for treatment-refractory patients is the internalization of new forms of object relatedness (13, 14, 27). If the relationships provided for internalization are part-object representations that mirror the patient's internal splitting processes, the treatment will merely solidify and confirm the patient's internal object world. On the other hand, if balanced, integrated relationships (containing both positive and negative aspects) are presented to the patient for internalization, the therapeutic task of integration becomes much more realistic and attainable.

Both caregivers and insurance companies have legitimate concerns. Hospitalization is costly. On the other hand, inadequately treated psychiatric illness may be devastating. Clinical and economic decisions regarding optimal length of stay are further hampered by the lack of definitive outcome studies on the cost effectiveness of extended hospital treatment. Negotiation and compromise—such as the trend toward increasing utilization of partial hospital settings—are sorely needed. A spirit of collaboration between payer and provider is the key to serving the patient's best interests.

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Psychological Comorbidity and Length of Stay in the General Hospital

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Objective: As general hospitals search for ways to cut costs without sacrificing efficiency, particular attention has been focused on factors that may prolong hospital stay. The results of prior studies that have reported an association between psychological and psychiatric comorbidity and longer hospital stays have been subject to different interpretations because of methodological design flaws. The current paper reports on a study of psychological comorbidity and length of stay that has been designed to avoid the methodological problems of earlier investigations. Method: The study was performed at a 429-bed tertiary-care, university-affiliated, voluntary, teaching hospital. During hospital days 3 to 5, patients were tested as available with the Mini-Mental State examination, the Zung Depression Inventory, and the SCL-90 and were rated for physical impairment with the Karnofsky Performance Status Scale. Statistical analyses were performed for correlations between length of stay and test scores, rating scales, and demographic and discharge data from the chart. Results: Of 424 patients approached, 321 (76%) agreed to participate and 278 (65.6%) completed the test battery. Depression, anxiety, and organicity, measured by psychological tests, were significantly correlated with longer hospital stay. These correlations remained significant after the authors controlled for degree of physical impairment, emergency versus elective admission, and medical versus surgical service, which were themselves correlated with longer hospital stay. Discussion: This study confirms a significant correlation between psychological comorbidity and length of stay after correcting for the methodological pitfalls found in earlier studies. The clinical, research, economic, and policy implications of these findings are discussed.

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In response to the rekindled interest in factors influencing extended length of stay and its economic implications, a number of recent studies have reexamined the association between psychiatric comorbidity and longer stay first reported by Billings (1) almost 50 years ago (2–11). While the evidence of a strong association between psychiatric comorbidity and longer hospital stay has grown, three important issues about the nature of that association have not been sufficiently addressed by this body of work. The first is whether psychiatric comorbidity precedes and, therefore, may contribute to extended hospital stays or whether it arises later after hospitalization has been prolonged by other factors. The second is whether or not length of stay and psychiatric comorbidity are directly correlated with each other or whether they covary with the degree of physical impairment. Third, all of the studies that reported a significant correlation were based on a small subgroup of the total population of patients with psychiatric morbidity who were spontaneously identified or referred by their medical or surgical physicians.

In the first of several retrospective studies, Dvoredsky and Cooley (2) reviewed 37,000 Veterans Administration hospital discharge charts and found a significant correlation between psychiatric comorbidity and length of stay. Fulop and co-workers (4) reported that the 5% of patients with comorbid psychiatric diagnoses found in the 59,000 charts they reviewed had significantly longer hospital stays. Lyons et al. (5) found significantly longer stays for patients with head and spinal cord trauma and psychiatric comorbidity in both the acute and rehabilitation phases of their hos-

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pitalization, while Cushman (8) found longer stays for stroke patients with depression and organic brain syndrome.

Because of their retrospective designs, these studies could not determine whether psychiatric comorbidity preceded and may have contributed to extended hospitalization or occurred later during the course, perhaps as a result of prolonged hospitalization. One attempt to deal with this methodological issue statistically still left the association unclear (7). Brezel et al. (9) found that burn patients with a prehospitalization history of substance abuse or mental impairment had a significantly longer hospital stay than other patients. However, they did not control for age or flame burns, both of which were greater in the study group.

Four prospective studies addressed some of the methodological limitations described previously. Levenson et al. (3) tested 80 consecutively admitted patients with a psychological battery but failed to find significant correlations between psychological test scores and subsequent length of hospital stay. Rogers et al. (10) failed to find a significantly longer stay for patients diagnosed with delirium on the fourth day after orthopedic surgery. In another prospective study, Morris and Goldberg (11) failed to demonstrate a relationship between psychological or psychiatric comorbidity and length of stay in gastroenterology patients with mixed diagnoses or a single diagnosis; this finding may be due to small sample size. However, Thomas et al. (6) did find that a diagnosis of delirium was associated with a longer stay.

Unfortunately, none of the cited studies with positive findings controlled for severity of physical impairment. Severity of physical illness and impairment have been found to strongly correlate with both longer stay (12) and greater psychiatric morbidity (13). In the study by Thomas et al. (6), the group of patients with delirium had a higher mortality rate than the control group. Since delirium is often seen as a harbinger of terminal states (14, 15), which may be associated with prolonged hospital stays, the longer stay may have been due to the greater physical morbidity of these patients. A similar issue can be raised regarding the retrospective study by Fulop et al. (4). In that study, it also is not clear whether severity of physical illness might have contributed to the longer stay, since patients with psychiatric comorbidity had a greater number of medical diagnoses, surgical consultations, and surgical procedures and a higher mortality rate.

All of the cited studies with positive findings relied on psychiatric diagnoses recorded by surgical or other nonpsychiatric physicians in the discharge summary or on spontaneous referral for psychiatric consultation. Psychiatric disorders are known to be underdiagnosed and patients with these disorders underreferred (1, 6, 16, 17) in the general hospital. One study demonstrated that only 10% of the population with psychiatric comorbidity were referred (16). Even when patients with psychiatric disorders are diagnosed and referred, the psychiatric diagnoses are frequently not reported in the discharge summaries (18). Studies using discharge psychiatric diagnoses or spontaneous referral to define psychiatric comorbidity report on results taken from a small subsample of patients who may be more likely to provoke referral and may not be representative of the population with psychiatric comorbidity.

The current paper reports on a study of psychological comorbidity and length of stay designed to avoid the methodological problems of earlier investigations. This prospective study used psychological tests administered to patients during days 3 to 5 and controlled for the severity of physical impairment and other potentially confounding variables.

METHOD

The study was carried out from June 1, 1985, through June 30, 1986, at Long Island Jewish Hospital, a 429-bed-tertiary care, university-affiliated, voluntary, teaching hospital. Patients from the four medical floors, four surgical floors, and one gynecology floor were tested as available on weekdays during the third to fifth hospital days. In order to address the potential bias of nonresponders, length of stay and other demographic data were also recorded for those patients who refused to participate or who agreed to participate but were excluded for the reasons described later. The test battery included a modified version of the SCL-90 (questions 13, 47, 70, and 80 were deleted because they were not appropriate for hospital inpatients—e.g., they dealt with phobic concerns on buses and subways in the prior week), the Zung Depression Inventory, and the Mini-Mental State examination. At the time of testing, each patient's nurse rated the degree of physical impairment according to the Karnofsky Performance Status Scale (19).

After each patient's discharge we gathered data from the chart on social and environmental factors that might affect length of stay, such as preadmission employment status, preadmission and postdischarge living arrangements, availability of postdischarge care, availability of significant others on discharge, and limitation of activity as prescribed by the physician. We also recorded type of admission, final diagnoses, and other demographic data.

RESULTS

Of 424 patients approached, 321 (76%) agreed to participate in the study. Thirty-four (10.6%) of the patients who agreed to participate had to be excluded before testing—21 because they were too physically ill, two because they were too emotionally ill (one was confused and one schizophrenic), eight because of language problems, and three for miscellaneous reasons. An additional nine (2.8%) were excluded after they failed to complete the test battery—three because they were too physically ill, one because of emotional upset, and five for miscellaneous reasons. A total of 278 patients, 65.6% of those initially approached, completed the test battery and made up the group of subjects studied.

Subjects ranged in age from 18 to 83 years (mean±SD=48.1±16.2). The mean length of stay was 8.7±6.7 days (range=3–61). Fifty-four percent (N=150) were women; 89% (N=247) were white; 42% (N=117) were Catholic, 35% (N=97) were Jewish, and 16% (N=44) were Protestant; 67% (N=186) were married; and 9% (N=25) were unemployed or disabled, 28% (N=78) were retired or homemakers, and 53% (N=147) were employed. Ninety-six percent (N=267) lived in their own home or apartment, and only 11% (N=31) lived alone.

The mean Zung depression score of the study group was 45.8±10.4; 9% (N=25) had moderate to severe depression (scores of 60 and above), while 34% (N=95) had minimal to severe depression (scores of 50 and above). The mean Mini-Mental State score was 27.3±2.3. We used a cutoff score of 23 or below (previously shown to have an 87% sensitivity and 82% specificity [20]) and found that 8% (N=22) of the patients had organic impairment according to the Mini-Mental State examination. The mean Karnofsky score was 72.9±15.7 (out of a possible 100); this score indicates that the patient can care for himself or herself but is unable to carry on normal activity or do active work. Since SCL-90 scores were not compatible with norms because of the deletion of four items inappropriate for hospitalized patients, only correlations will be reported for these data. The group of patients who refused to participate or who agreed to participate but had to be excluded for the reasons described earlier were significantly older than the study group (61.2±17.5 versus 48.1±16.2 years; t=7.62, df=379, $p<0.001$) and stayed significantly longer (13.8±14.5 versus 8.7±6.7 days; t=2.52, df=378, $p<0.01$).

A two-tailed alpha value of 0.05 was used to determine significance. Significant correlations between length of stay and test battery scores were found. A parallel analysis was done on the log transformation, with results similar to those reported later. Longer stay was significantly correlated with greater organicity on the Mini-Mental State (r=−0.17, df=275, p=0.004), with higher depression scores on the Zung Depression Inventory (r=0.13, df=276, p=0.03), and with higher depression and anxiety scores on the subscales of the SCL-90 (r=0.13, df=274, p=0.04, and r=0.12, df=274, p=0.05, respectively). A trend was evident (r=0.11, df=274, p=0.05) for the psychoticism subscale. Greater physical impairment, as measured by the Karnofsky Performance Status Scale, was also significantly correlated with a longer stay (r=−0.22, df=276, p=0.001) and with greater psychological morbidity (organicity on the Mini-Mental State [r=0.13, df=275, p=0.03] and on the depression, paranoia, and obsessive-compulsive subscales of the SCL-90, with a trend for depression on the Zung Depression Inventory [r=−0.10, df=276, p=0.09]). When Karnofsky ratings of physical impairment were controlled for, significant correlations with length of stay were again obtained for organicity on the Mini-Mental State (r=−0.14, df=274, p=0.02) and depression on the Zung Depression Inventory (r=0.13, df=275, p=0.03) and the anxiety subscale of the SCL-90 (r=0.12, df=273, p=0.04), while the depression and psychoticism subscales of the SCL-90 showed trends in the same direction (r=0.10, df=273, p=0.09, in both cases).

Other variables were also found to be associated with longer stay. Patients admitted on an emergency basis stayed longer than patients admitted on an elective basis (9.7±8.0 versus 7.3±3.9 days; t=3.30, df=248, p=0.001). Medical patients stayed longer than surgical patients (10.6±10.3 versus 7.9±4.6 days; t=2.10, df=80, $p<0.05$). When type of admission was controlled for, the Mini-Mental State again showed a significant correlation (r=−0.15, df=274, p=0.02), as did the Zung Depression Inventory (r=0.14, df=275, $p<0.02$) and the anxiety subscale of the SCL-90 (r=0.13, df=273, $p<0.04$), while the depression subscale of the SCL-90 showed a trend (r=0.12, df=273, p=0.05). When service (medicine versus surgery) was controlled for by stratifying on service, the pattern of results relating psychological test scores with length of stay did not differ from the results reported earlier for the combined sample.

No associations with length of stay were found for age, discharge medical diagnosis, preadmission living arrangements, occupational status, day of testing, discharge condition, limitation of activities on discharge, or other psychosocial factors. The high percentage of patients in our study who were admitted from, and discharged to, their own homes prevented a meaningful analysis of the correlation of type of dwelling with length of stay. Older age was not correlated with longer stay, but it was correlated with greater psychological morbidity on the Mini-Mental State and the subscales of the SCL-90.

When 30 patients staying more than 14 days (outliers) were compared with the rest of the study population, which stayed 14 days or less, a significant difference was found in organicity, as measured on days 3 to 5 by the Mini-Mental State (t=2.17, df=33, p=0.04). Despite the finding of more organicity, these patients were not more physically impaired at the time of testing than were patients who stayed 14 days or less.

When the 30 patients who stayed longer than 14 days were excluded from the correlational analysis, the correlations of psychological test scores with length of stay lost significance. However, the patterns of correlations within the two groups were similar. Sensitivity was 50%, specificity 68%, and accuracy 66%. Because of the difficulty of interpreting the correlations in the presence of outliers, a nonparametric approach was taken.

Scores on all nine subscales of the SCL-90 were higher in the group of 30 outliers than in the other 248 patients. While most differences were not significant, the pattern of results, as measured by the nonparametric sign test, indicates a clear relationship between length of stay and psychological comorbidity ($p<0.01$). Consistent with these results, when the Zung score was dichotomized at ±50 and cross-tabulated with length of stay dichotomized at ±2 weeks, a significant difference was found ($\chi^2=3.94$, $df=1$, $p<0.05$). When the Mini-Mental State score was similarly dichotomized at ±23, a significant difference was found ($\chi^2=3.50$, $df=1$, $p=0.06$).

Eight of 278 patients (2.9%) in the study group had psychiatric consultations. Although their stay was twice as long as that for patients without consultations (17.1±15.5 versus 8.4±6.1 days), the difference was not statistically significant.

Psychiatric consultations were significantly correlated with ratings on the three psychological scales; with the mean SCL-90 and obsessive-compulsive, interpersonal sensitivity, depression, anxiety, paranoid ideation, and psychoticism subscales; with organicity on the Mini-Mental State; and with moderate to severe depression (score of 60 or above) on the Zung Depression Inventory. However, only three (14%) of the 22 patients with scores indicating organicity on the Mini-Mental State and three (12%) of the 25 patients with moderate to severe depression on the Zung Depression Inventory were referred for psychiatric consultation.

Psychiatric discharge diagnoses were recorded on the charts of only five patients (1.8%). There was no significant difference in length of stay between these patients and the rest of the subjects.

DISCUSSION

This paper describes a prospective study of psychological comorbidity and length of hospital stay that controlled for severity of physical impairment and other potentially confounding variables such as type of admission (emergency versus elective) and type of hospital service (medical versus surgical). In this study, psychological scores obtained on previously validated, reliable instruments indicated that greater levels of depression, anxiety, and organicity during days 3 to 5 of hospital stay were associated with longer stay. Further, psychological test scores were found to be significantly worse in a subset of outlier patients staying more than 14 days.

The use of psychological screening scores may more accurately reflect the full extent of psychiatric comorbidity in this population than discharge diagnoses in the chart or the records of psychiatric consultations, which are known to underrepresent psychiatric illness (1, 6, 16–18). The Mini-Mental State examination (20, 21) and the SCL-90-R (22–24) have previously been tested for validity and specificity in medical inpatients. The Zung Depression Inventory correlates with the depression scale of the SCL-90 and has been used to screen for depression in primary practice (25). It is important to recognize, however, that while psychometric tests have the advantage of screening a broad sample of inpatients and even though test scores may correlate with clinical psychiatric diagnoses, they are not equivalent to them.

In other studies, only 14% of depressed inpatients (13) and 37% of cognitively impaired patients (26) (according to psychometric test results) were recognized by medical residents, and only 11%–12% of medical inpatients with significant psychiatric comorbidity are referred for consultation (16, 27). In the current study, only 12% of patients with psychologically significant depression and 14% with organicity were referred. While 2.9% of the study group were referred for psychiatric consultation, only 1.8% had psychiatric discharge diagnoses. Had our study relied just on psychiatric consultations or psychiatric discharge diagnoses on the charts, no significant correlation with length of stay would have been found.

The rates of psychologically significant depression and severe depression found in our study—34% and 9%, respectively—are consistent with other reports, which show ranges of 15%–36% and 8%–14%, respectively (13, 26, 28).

The problem of defining clinical depression in medical patients has been well described (28–31). It has been suggested that physical illness may spuriously elevate rating scale scores for depression by contributing to symptoms of fatigue, anorexia, and insomnia. Nevertheless, these symptoms can still serve as valid indicators of depression (32). In our study, the association of depressive scores with length of stay persisted even when severity of physical impairment was controlled for.

The relatively low 8% prevalence of organicity that we found, compared to the 28%–34% reported in other comparable studies (20, 26), may reflect inherent differences in the population studied, such as age, education, or other factors or the time of testing during the hospital stay. A higher proportion of older patients, who are more likely to have organic impairment (15, 33, 34), refused to participate or were excluded from our study, some because of the severity of their organic brain syndrome. In addition, by testing during days 3 to 5, we might have missed a significant number of elderly patients who became organically impaired later in their hospitalization (6, 15).

The Karnofsky Performance Status Scale as a measure of severity of physical impairment was, as expected, strongly correlated with longer stay and with more psychological morbidity. These findings are consistent with results obtained with other measures of severity of physical illness (12, 13).

Our findings emphasize the need to develop practical screening approaches and clinically sound therapeutic interventions that are effective in reducing length of stay. Zook and Moore (35) also called for the development of effective interventions for a defined group of high-cost inpatient users of medical services in order to diminish their disproportionately long hospital stays. Patients with psychiatric problems make up a significant portion of this group. The significant impact of depression on days spent in bed and on impairing functioning in medical outpatients has been persuasively demonstrated in the medical outcomes study (36), which also showed that the effect of depression is additive in patients with physical comorbidity.

The manner in which organicity, depression, and anxiety may contribute to longer stay cannot be determined from our data. However, the clinical literature offers some insights from case reports. In their intervention study Levitan and Kornfeld (37) described several delirious patients awaiting institutional placement who were able to be discharged to their homes after proper diagnosis and treatment. Anxiety and depression can confuse the diagnosis and lead to more extensive and time-consuming tests and may impede the patient's participation in (37), and response to, treatment. In addition, unresolved family conflicts (38), iatrogenic psychiatric illness (37), borderline personality disorders (39), and somatoform disorders (1, 17, 38, 40) have all been reported as preventable causes of extended hospital stays.

Psychiatric consultation-liaison programs have not ordinarily been viewed as economically effective services capable of reducing hospital costs in the population with psychiatric comorbidity (41). The fact is that the clinical cost effectiveness of consultation-liaison services has not been definitively investigated, although preliminary studies suggest that psychiatric interventions provided by them are clinically effective (17, 42) and economically sound (1, 37). Significant economic benefits have been amply demonstrated for psychiatric intervention in other areas of medical care (43, 44).

Levitan and Kornfeld (37) and Strain et al. (45) have demonstrated significant savings from a consultation-liaison program for elderly patients with hip fractures. One study (42) showed a trend for a shorter stay with psychiatric consultations. Another study (46) actually found that patients receiving psychiatric consultations had longer stays. However, the latter study did not have an adequate control group and did not determine whether psychiatric comorbidity and consultation may have been the result rather than the cause of extended stays. In this context, two studies (5, 47) found that the earlier the psychiatric consultation, the greater the reduction in length of stay both in absolute terms and relative to the time of consultation.

The problem of early detection of patients with psychiatric comorbidity looms large. While we found a significant association between greater psychological comorbidity and longer stay, sensitivity and specificity were limited. Further work needs to be done to determine whether the specificity and sensitivity of screening methods can be improved to the point where they can serve as practical guides for clinical intervention trials.

While we cannot on the basis of this study recommend an optimal test battery, we can suggest that psychometric instruments used in the identification of psychiatric comorbidity possess certain characteristics. They must be objective, reliable, and valid for the general hospital population and should take into account the patient's psychosocial functioning and degree of impairment. Since even an hour of testing may be too long for a significant proportion of inpatients, tests should be brief and easy to administer and score.

Whether active liaison (16, 17), psychological screening, or some combination of the two turns out to be the most effective way to detect patients with psychiatric comorbidity who are at risk for longer hospital stays remains to be seen. Preliminary results from our institution suggest that multimodal screening approaches may offer a practical way to identify a subpopulation of patients in whom psychological factors have a greater association with longer stay.

As the weight of evidence increasingly points to a direct association between psychological comorbidity and longer stay, the need becomes more pressing than ever to examine through methodologically sound studies the possible therapeutic and fiscal benefits of treatment intervention in patients with psychiatric comorbidity. Psychiatric consultation-liaison services, because of their joint functions of detection and intervention with such patients, are well positioned to engage in these research endeavors. It is only with the benefit of data derived from such studies that legislators and administrators can fashion enlightened health policies to address the clinical and economic impact of psychological comorbidity in general hospital patients.

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Housing Instability and Homelessness Among Rural Schizophrenic Patients

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Objective: The authors examined housing instability among treated schizophrenic patients in a rural area and compared the findings with those from their previous study of urban patients. Method: Seventy-five patients with schizophrenia or schizoaffective disorder who were treated in a rural mental health center were assessed with research interviews and ratings by their clinical case managers. The patients were followed for 1 year to identify episodes of psychiatric hospitalization, incarceration, and literal homelessness. Results: Of the 75 patients, 19 (25%) had housing situations characterized as unstable by their case managers. For the majority, housing instability signified tenuousness of living arrangements rather than literal homelessness. Noncompliance with medications, alcohol use, and negative symptoms accounted for 30% of the variance in unstable housing. During follow-up, the unstably housed patients, compared to those in stable living situations, were no more likely to be rehospitalized but were somewhat more likely to be jailed and significantly more likely to be literally homeless. Conclusions: In the authors' previous study of urban psychiatric patients, unstably housed patients were more likely to be literally homeless, highly symptomatic, and rehospitalized during follow-up than the rural patients with unstable housing. Better outcomes in the rural area appeared to be related to the greater availability of housing alternatives and to intensive case management. For patients with unstable housing in both settings, noncompliance with medications and substance abuse, as well as housing arrangements, should be assertively addressed.

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Approximately one-third of the people who are literally homeless have severe mental illnesses (1). Among the severely mentally ill in the community, however, literal homelessness represents only an extreme on the continuum of residential instability. Many who are not literally homeless live in stressful, substandard, or transient circumstances that can be considered unstable. Urban housing instability is associated with poor adjustment and predisposes not only to homelessness but also to institutionalization in jails and hospitals (2–4). In our previous work with aftercare patients of an urban state hospital (4), we found that housing instability was strongly correlated with abuse of alcohol and street drugs, noncompliance with treatment, psychosocial problems, and a variety of psychiatric symptoms. Urban patients with unstable housing were literally homeless much of the time, were attracted to the hospital as a living alternative, and were nearly twice as likely to be rehospitalized during 1-year follow-up. Housing instability in urban areas may be an important mediating variable that signals a shift from stable community adjustment to literal homelessness, attraction to the hospital, and institutionalization.

Little research has been done on housing instability and homelessness in rural areas. According to an Institute of Medicine report (5), the homeless in rural areas are typically not gathered in group living sites, such as shelters; instead, they are temporarily housed with family, friends, or neighbors but lack the resources to secure permanent housing. To our knowledge, the extent and significance of housing problems among the mentally ill in rural areas have not been studied. Do housing problems predispose them to poor

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adjustment, literal homelessness, attraction to the hospital, and institutionalization?

As part of our clinical research program on dual diagnosis and homelessness (6, 7), we examined the meaning, correlates, and consequences of housing instability for treated schizophrenic patients in a rural area and compared these findings with those from our previous study in an urban area (4), which was conducted with similar methods. Our hypothesis was that the rural schizophrenic patients would have a lower prevalence of literal homelessness than the urban patients but that the rural patients who did have unstable housing situations would also manifest poor adjustment and negative outcomes.

METHOD

Subjects

The subjects for this study were schizophrenic outpatients treated in a comprehensive community mental health center (CMHC) affiliated with a university medical school in rural New England. All active cases during 1987 involving outpatients with clinical diagnoses of schizophrenia or schizoaffective disorder were considered for the study. Two research psychiatrists (including R.E.D.) screened CMHC records, interviewed patients according to *DSM-III-R* criteria, and excluded 15 patients with inaccurate or questionable diagnoses. Of the remaining 79 patients with definite *DSM-III-R* schizophrenia or schizoaffective disorder, 75 consented to participate in a research interview about their adjustment.

The final study group of 75 patients had a mean±SD age of 43.6±14.3 years; 48.0% were men, and 52.0% were women. All were Caucasian. Only 14.7% of the patients were currently married; 60.0% were single, and 25.3% were separated, divorced, or widowed. The total time spent in any mental hospital before the interview ranged from a few months to 40 years (median=9 months). The distribution of *DSM-III-R* diagnoses was as follows: schizophrenia, 89.3% (N=67), and schizoaffective disorder, 10.7% (N=8). All of the subjects were followed closely by clinical case managers who had low caseloads (fewer than 35), training in substance abuse assessment, opportunities to make frequent behavioral observations in the community, and access to collateral information from families, community contacts, and other caregivers.

Setting

The local CMHC provides comprehensive services to the severely mentally ill in a rural catchment area of approximately 85,000 residents. During the study period, a range of housing options—supervised group homes, scattered-site apartments, crisis apartments, and low-cost housing—was available to this group of patients. The local CMHC operates and supervises 40 residential placements for approximately 200 severely mentally ill patients. Since nearly all patients have families in the area, the available beds are usually sufficient. This situation contrasts with that in many large urban areas, in which only a small percentage of the severely mentally ill have access to suitable housing arrangements (8).

Procedures and Measures

The subjects were assessed by means of a combination of research interviews and clinician ratings. The interviews were conducted by researchers (including T.S.P.) using standardized instruments. Clinical case managers independently rated the patients on psychosocial variables and psychiatric symptoms after receiving individual training with our case manager assessment instrument. Interrater reliability, described in detail elsewhere (4, 9–12) and assessed again with subgroups of patients in this study, was high. The subjects were followed up 1 year after the initial evaluation.

The stability of the patients' living arrangements in the community over the previous 6 months was rated by case managers on a 5-point scale, ranging from "highly supportive" to "highly stressful"; each point on the scale was anchored by a brief example (4). Subjects with "stressful" and "highly stressful" living arrangements (points 4 and 5) were classified prospectively as having unstable housing. After making these ratings, the case managers responded to open-ended, semistructured interviews about the subjects' housing instability, number of recent moves, episodes of literal homelessness, causes of housing problems, and supports needed to maintain housing.

Alcohol and other drug use was assessed through a combination of hospital records, research interviews with standard instruments, case manager ratings, and intensive case reviews (9). The patient interview included the Alcohol Dependence Scale (13) and other standard tests and items. The case managers rated alcohol and other drug use according to 5-point clinician rating scales (9, 11, 12) developed specifically for this population. Consensus *DSM-III-R* diagnoses of alcohol use disorder were based on a combination of these methods (9).

The case managers rated seven psychosocial variables (shown in table 1) on 5-point scales ranging from "highly significant" support/strength to "highly significant" stressor/weakness. The variables were defined with narrative anchor points and dualistically—as a support/strength or as a stressor/weakness—because we believe they represent interactions between patients' capacities and their environmental conditions (14).

Psychiatric symptoms were evaluated through a combination of research interviews and case managers' ratings. Research interviewers (including T.S.P.), blind to other information, conducted structured interviews that included the Hamilton Rating Scale for Depres-

TABLE 1. Clinical Variables Among Rural Schizophrenic Outpatients Whose Housing Situations Were Stable or Unstable

	Housing in 6 Months Before Evaluation				Correlation	
	Stable (N=56)		Unstable (N=19)			
Variable	N	%[a]	N	%[a]	Kendall's tau-c	p
Psychosocial problems[b]						
Food	9	16.1	5	26.3	0.24	0.003[c]
Finances	27	48.2	14	73.7	0.27	0.001[d]
Daily activities	12	21.4	9	47.4	0.31	<0.001[d]
Social relationships	24	42.9	14	73.7	0.21	0.01
Family relationships	20	35.7	15	78.9	0.27	0.002[c]
Caregiver relationships	7	12.5	5	26.3	0.06	0.23
Medication compliance	13	23.2	14	73.7	0.27	0.001[d]
Current substance use						
Alcohol Dependence Scale[e]	6	10.7	7	36.8	0.31	<0.001[d]
DSM-III-R diagnosis of alcohol abuse or dependence						
Interview	6	10.7	8	42.1	0.24	0.001[d]
Consensus	9	16.1	10	52.6	0.27	<0.001[d]
Case manager rating[f]						
Alcohol	9	16.1	9	47.4	0.27	<0.001[d]
Drugs	3	5.4	3	15.8	0.15	0.002[d]
Clinician-rated symptoms[f]						
Hostility	9	16.1	3	15.8	−0.02	0.42
Suicidal ideation	2	3.6	4	21.1	0.18	0.004[c]
Bizarre behavior	22	39.3	9	47.4	0.14	0.06
Hallucinations/delusions	30	53.6	14	73.7	0.06	0.25
Suspiciousness/paranoia	26	46.4	11	57.9	0.06	0.24
Depression	17	30.4	7	36.8	0.11	0.11
Negative symptoms	21	37.5	10	52.6	0.17	0.03
Conceptual disorganization	12	21.4	6	31.6	0.14	0.06
Self-reported psychotic symptoms						
Auditory hallucinations	31	58.5	13	68.4	0.15	0.12
Paranoia	19	35.8	9	47.4	0.05	0.34
Thought broadcasting	19	35.8	11	57.9	0.27	0.02
Telepathic delusions	25	47.2	11	57.9	0.17	0.09
Thought insertion	22	41.5	12	63.2	0.27	0.02
Ideas of reference	21	39.6	10	52.6	0.08	0.26
Suspiciousness	25	47.2	9	47.4	0.00	0.49
Derealization	14	26.4	5	27.8	−0.10	0.21
Nihilistic delusions	14	26.4	6	35.3	−0.01	0.46
Interviewer-rated depressive symptoms						
Total Hamilton score ≥13	19	35.2	8	47.1	0.15	0.05
SCID-P						
Major depression	4	7.5	3	16.7	0.04	0.31
Dysthymia	4	8.0	4	26.7	0.18	0.03

[a] For self-reported and interviewer-rated symptoms, percentages based on varying Ns because some subjects did not complete all of the interview.

[b] Score of 4 or 5 on 5-point scale.

[c] Significant at $p<0.05$ after Bonferroni adjustment.

[d] Significant at $p<0.01$ after Bonferroni adjustment.

[e] Score of 5 or more on 47-point scale.

[f] Score of 3 or more on 5-point scale.

sion (15), the affective disorders section of the Structured Clinical Interview for DSM-III-R—Patient Version (SCID-P) (16), questions to determine self-reported presence or absence of nine typical psychotic symptoms (shown in table 1), and selected items from the Alcohol Use Inventory (17).

Each patient's case manager rated eight psychiatric symptoms (shown in table 1) according to the patient's characteristic condition while in the community over the previous 6 months. The symptoms were rated on 5-point scales that ranged from "not present" to "extremely severe." The clinician rating scales, developed by modifying items from the Brief Psychiatric Rating Scale (18) and the Scale for the Assessment of Negative Symptoms (19), and their validation are described in more detail elsewhere (4, 11, 12, 20).

Living preference was defined as the patient's attitude toward the hospital as a place to live compared with his or her current housing in the community (10, 21). The case managers were asked to classify each patient's living preference as "hospital attraction" or "community attraction" according to the patient's attitudes and behaviors rather than severity of illness or need for hospitalization.

The patients were followed prospectively for 1 year to identify episodes of psychiatric hospitalization, incarceration, and literal homelessness. A research assistant (T.A.C.) identified and verified all episodes by interviewing case managers, examining CMHC records, and checking discharge summaries, hospital records, and public records of incarceration directly. For subjects with unstable housing at the time of the baseline assessments, the course of housing stability was examined qualitatively by interviewing all treatment and housing personnel involved in each patient's care during the follow-up year.

Statistical Analyses

We used Kendall's tau-c (22), a robust measure of association for ordered categorical data, to estimate the correlations between ordered variables. When several bivariate correlations were tested together, we conservatively adjusted significance levels using the Bonferroni correction (23). We modeled correlates of housing instability using ordinary least squares multiple regression techniques that have been recently shown to be robust for ordered categorical data (24). We estimated a multiple regression model by an "all possible" regressions procedure followed by a residual analysis (25, 26). For nominal outcome variables with few observations, we assessed associations with Fisher's exact test.

RESULTS

Housing Instability and Correlates

Only four subjects (5.3%) were rated as having "highly stressful" housing situations during the evaluation period, and 15 (20.0%) were considered to have "stressful" housing arrangements. Thus, 19 subjects (25.3%) had experienced housing instability during the 6 months before assessment, and the remaining 56 (74.7%) had stable housing.

Qualitative interviews of the case managers indicated that the four subjects with "highly stressful" housing situations were intermittently experiencing literal homelessness. Two were under restraining orders by the relatives they had been living with because of violent behavior and were in shelters. One had been evicted from an apartment and was staying occasionally with friends and in a shelter at other times. The fourth left a group living situation and was wandering between different relatives' homes and shelters.

Of the 15 subjects with "stressful" housing arrangements, five were in the process of being extruded from their living situations because of behavioral or financial conflicts with landlords or families. Five subjects were experiencing tension with landlords or families, also because of behavorial or financial strains, but were being maintained in their current situations with intensive support from their case managers. Four subjects who had been in stressful housing situations were making planned moves to more desirable living situations. One elderly subject required extensive assistance because of medical problems and was constantly in danger of losing her independent living situation. None of these subjects had experienced literal homelessness.

Housing instability was not related to the background variables of age, sex, marital status, and past hospitalization. It was, however, strongly related to several psychosocial problems. Table 1 shows that about three-quarters of the unstably housed subjects had problems with finances, social relationships, family relationships, and medication compliance. Among psychosocial variables, only relationships with caregivers was clearly nonsignificant.

Table 1 also indicates that measures of current alcohol use, whether determined by means of case manager ratings, structured interviews, or consensus diagnoses, were highly related to housing problems. Other drug use, which was almost exclusively marijuana use in this group (27), was also related to housing instability. According to their self-reports, all of the subjects with both alcoholism and unstable housing had developed drinking problems first. To assess further the relationship between the two variables, we used consensus diagnoses to compare the 19 subjects who had active alcohol use disorders with the 19 subjects whose alcohol use disorders were in remission during the previous year. Active alcohol problems were strongly correlated with housing problems (Kendall's tau-c=0.45, p=0.008); the subjects with remitted drinking problems had only a 16% rate of housing instability (N=3), which was equal to the rate among nonalcoholics in the group.

Table 1 also shows, by contrast, that psychiatric symptoms generally did not correlate with housing instability, regardless of whether the symptoms were determined by means of clinician ratings or interview. The one exception was suicidal ideation. A higher proportion of subjects with unstable housing were seen as suicidal by clinicians, a result validated by the finding that they scored higher on the suicide item of the Hamilton depression scale (Kendall's tau-c=0.21, p=0.002). A few other items showed nearly significant correlations, but with this small number of subjects, the correlations were not significant after Bonferroni adjustment.

Only two subjects in the entire group, both with unstable housing, were classified as "attracted to the hospital" as a living alternative. Although the number was too small to relate hospital attraction to housing status, it substantiates the lack of hospital attraction in this rural group.

We estimated a multiple regression model for housing instability (5-point scale) by including background variables and current adjustment variables that could logically underlie housing problems but excluding psychosocial variables, such as problems with food and

TABLE 2. Multiple Regression Equation for Housing Instability Among 75 Rural Schizophrenic Outpatients[a]

Variable in Equation	Parameter Estimate	SE	p
Medication noncompliance	0.25	0.08	0.004
Alcohol use[b]	0.35	0.12	0.005
Negative symptoms	0.25	0.11	0.02
Intercept	0.56	0.37	0.13

[a]Computations based on SAS PROC REG program (26).
[b]Based on 5-point case manager ratings.

finances, that are logically redundant with housing problems. The model contained just three variables: medication noncompliance, alcohol use, and negative symptoms. The estimated coefficients with standard errors and p values are shown in table 2. Taken together, these three variables accounted for 30% of the variance in housing instability.

Residential Outcome

Data on hospitalization, incarceration, and literal homelessness during the year after initial evaluation are shown in table 3. One subject moved out of state during the year and was lost to follow-up. Compared with those in stable housing situations, the subjects with unstable housing had a similar rate of rehospitalization, a slightly higher rate of incarceration, and a significantly higher rate of literal homelessness.

Qualitative interviews at 1-year follow-up for the 19 subjects initially classified as having unstable housing revealed the following. Of the four subjects who had been in "highly stressful" housing situations, one was jailed for domestic violence, moved to an urban area and became literally homeless, and was eventually jailed for assaulting a police officer. A second was literally homeless for several weeks but spent most of the year in jail as a result of domestic and community violence. A third continued to alternate between transient residences (at least five separate locations) and literal homelessness. The fourth subject continued to wander between various relatives' homes, spent about one-fourth of the year literally homeless, and was hospitalized once. All four presented severe behavioral problems related to noncompliance with medication regimens and substance use disorders.

The 15 subjects who had experienced "stressful" housing had more varied residential outcomes during follow-up. Of the five who were extruded from their living situations because of conflicts with landlords or families, three were hospitalized (one after a brief episode of literal homelessness), four continued to have difficulties in their new situations because of similar problems, and all experienced subsequent moves. Four of the five who had been experiencing chronic tension with landlords or families remained in their strained situations with continued supports, and one of these four was hospitalized several times. The fifth subject died of cancer. The four subjects who made elective moves were all satisfied with their housing situations and remained stable. The elderly subject was hospitalized for medical problems and died soon thereafter.

TABLE 3. Residential Outcomes of Rural Schizophrenic Outpatients Whose Initial Housing Situations Were Stable or Unstable

Outcome During 1-Year Follow-Up	Housing in 6 Months Before Initial Evaluation: Stable (N=55) N	%	Unstable (N=19) N	%	p (Fisher's exact test, two-tailed)
Rehospitalization	10	18.2	4	21.1	0.75
Incarceration	1	1.8	3	15.8	0.05
Literal homelessness	0	0.0	5	26.3	0.001[a]

[a]Significant at $p<0.01$ after Bonferroni adjustment.

DISCUSSION

Even in a rural area with available housing alternatives and families nearby, one-quarter of our subjects had unstable living arrangements. However, only 5% experienced literal homelessness during the 6 months before baseline assessment, and these did so only intermittently. By contrast, of the urban subjects we studied previously (4), although a similar percentage (27%) had unstable housing, all of those with unstable housing were literally homeless, many for prolonged intervals, during a similar period.

Rural housing instability typically indicated tensions between the subjects and their landlords or families, tensions that threatened current housing arrangements, rather than literal homelessness. Case managers reported that housing problems were often related to alcohol abuse or noncompliance with medication regimens—an impression that was strongly supported by our multiple regression model.

Rural housing instability was strongly correlated with a variety of other psychosocial problems. These were not rated independently and were logically redundant with, or components of, housing instability. Rural subjects with unstable housing appeared similar to our urban subjects with unstable housing both in terms of psychosocial problems and in the extent to which alcoholism and medication noncompliance complicated their adjustment (4). These various urban/rural similarities in the correlates of housing instability testify to its significance in rural, as well as urban, settings, even though it was less severe among our rural subjects.

Several findings support the interpretation that alcohol use leads to housing instability rather than the other way around. First, all of our rural subjects with concurrent housing instability and alcohol use disorders stated that they had developed drinking problems before experiencing housing problems. Second, most of our subjects with precarious living arrangements nevertheless were not exposed constantly to the ravages of street life, including the ubiquitous presence of alcohol and other drugs. Third, the case managers reported that the subjects' landlords and families objected to behaviors related to alcohol use, so these behaviors directly threatened housing arrangements. Fourth, once alcohol use was included in our multiple regression equation, most of the other variables disappeared. Finally, the subjects with remitted alcohol use disorders, compared to those with active alcohol problems, showed little housing instability. Since current drinking problems are integral to housing instability, living arrangements that discourage drinking seem desirable (28, 29).

In contrast to our urban subjects, the unstably housed rural subjects did not manifest more severe symptoms. (Only suicidality was significantly related to housing instability.) This low level of symptoms is consistent with our findings that our rural subjects with unstable housing avoided long-term literal homelessness and that in our urban group only the subjects with prolonged literal homelessness exhibited extremes of psychiatric symptoms. The subjects in our rural group seem to have been protected from environmental stress of that magnitude. In the same vein, the rural subjects, even those who were unstably housed, did not seem to be attracted to the hospital as a living alternative, as were the urban homeless subjects (4), presumably because of the available housing options.

Rural housing instability was related to negative outcomes only minimally. The unstably housed subjects had a low rate of hospitalization, as did those with stable housing. A few unstably housed subjects were incarcerated, but the statistical significance was marginal, and the proportion was low. The subjects with intermittent episodes of literal homelessness continued in that pattern, but none developed prolonged homelessness, and only one additional subject experienced a brief episode of literal homelessness. Furthermore, qualitative follow-up interviews revealed that unstably housed subjects who were able to obtain more satisfactory housing avoided these negative outcomes. Clinical experience and interviews with case managers and subjects lead us to speculate that housing availability and assertive case management in rural areas are critical in preventing negative outcomes among severely mentally ill patients. We recognize, however, that rural mental health care differs from urban situations in many other aspects (30), which may be related to outcomes.

Housing instability, even when less severe, as in rural areas, remains an important signifier of risk. Our findings indicate that schizophrenic patients in rural areas who have unstable housing situations experience multiple psychosocial problems, have few supports, and exhibit dangerous behaviors, such as alcohol abuse and medication noncompliance, that increase their risk of literal homelessness. We believe that literal homelessness and institutionalization can be avoided if housing options are available and if case managers make assertive efforts to meet patients' housing and other needs, but these impressions should be confirmed by further research. Since alcohol abuse and medication noncompliance are strongly implicated as underlying factors, they should be vigorously addressed, in part by providing alcohol-free living arrangements. All of our findings support the primacy of stable housing for successful community treatment of the severely mentally ill.

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A Critical Appraisal of Mitogen-Induced Lymphocyte Proliferation in Depressed Patients

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Objective: *The authors' goal was to evaluate the utility of mitogen-induced lymphocyte proliferation assays in clinical research in psychoimmunology.* Method: *They examined 23 depressed patients and 23 matched comparison subjects with this assay. There were no significant differences between these groups. They then combined the results of this study with the results of their previous study of 20 depressed patients and 20 comparison subjects to examine possible determinants of lymphocyte proliferation in depression.* Results: *Depressed patients with lower proliferative responses than their matched comparison subjects had lower depression subscale, anergia subscale, and total scores on the Brief Psychiatric Rating Scale than did patients with higher proliferative responses than their matched comparison subjects. This finding was unexpected and unexplained. Depressed patients with lower proliferative responses than their matched comparison subjects also had fewer obsessions and compulsions and less psychomotor agitation according to the Schedule for Affective Disorders and Schizophrenia interview than did patients with higher proliferative responses than their matched comparison subjects. Stepwise discriminant analysis and cluster analysis contributed little further understanding of the determinants of in vitro lymphocyte proliferation of cells from depressed patients.* Conclusions: *Longitudinal studies using multiple serial determinations of mitogen-induced lymphocyte proliferation are the minimal design needed to make this assay useful in further evaluating any immune system changes in depression.*

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A century of only occasional interest in neuroimmunology has developed into an explosion of work and information in this area in the past decade. One facet of this recent research has been the description of immune cells and tissues in patients with major mood disorders. One focus of psychoimmunology during the past 12 years is the mitogen-induced proliferative response of peripheral blood lymphocytes from depressed patients. The literature on mitogen-induced lymphocyte proliferation is now in conflict.

The first study examining this question (1) did not find that psychotically depressed patients had different proliferative lymphocyte responses to mitogen than comparison subjects, whether the depressed patients were ill or in remission. Two other early studies (2, 3) described obviously lower proliferative responses in severely depressed patients than in comparison subjects, although no between-group difference was found when less depressed patients were compared with nondepressed subjects (4). Attempts at replication have not found such clear results (5), and more recent reexaminations of larger numbers of subjects have perhaps yielded valuable insights into the clinical variables affecting the findings (6). Our own group (7) reported equivocal conclusions of the effect of major depression on lymphocyte proliferation, based on a study of 20 depressed patients and 20 matched comparison subjects.

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In the current study we present a replication of our previous study using a different immunology assay method (bovine and autoserum supplementation rather than HB103 serum-free medium) with much the same equivocal results. We then report on an analysis of the two studies combined. One hypothesis tested in this study is that depressed patients with and without lower mitogen-induced lymphocyte proliferative responses are different in some clinical measure relevant to their mental state, such as Brief Psychiatric Rating Scale (BPRS) score or psychomotor retardation.

METHOD

Subjects

Since the last study, 46 new male subjects (23 patients and 23 age-matched comparison subjects) have been examined. The patients were recruited for admission to the National Institute of Mental Health Clinical Research Center from patients who came to a Veterans Administration (VA) medical center mental health clinic or psychiatric emergency service. As in the previous study (7), the patients were hospitalized of clinical necessity on a voluntary basis in the research center at our facility. All patients admitted to the research center who met the criteria listed here and gave informed consent were studied.

To be admitted to the study, patients had to be 21 to 75 years old and meet the following diagnostic screening criteria. All patients completed a Schedule for Affective Disorders and Schizophrenia (SADS) interview (8) conducted by a research fellow in psychiatry. (Individual items from the SADS are used in later analyses.) Research diagnoses were made in a consensus meeting of three psychiatrists using both the Research Diagnostic Criteria (RDC) (9) and *DSM-III-R* nosologic systems. All patients included had a diagnosis of major depressive disorder by RDC and of major depression by *DSM-III-R*. Subjects not meeting these diagnostic screening criteria were excluded. Severity of depression was measured by the Hamilton Rating Scale for Depression (10, 11), the Beck Depression Inventory (12), and the depression subscale of the BPRS. The physical health of all patients was assessed by medical history, physical examination, CBC, CHEM-20 blood chemistry profile, serum cholesterol and triglycerides, T_3, T_4, RPR, urinalysis, and ECG. Those with medical histories or conditions that would affect the results of this study were excluded. Number of years of education, cigarettes smoked per day, and cups of coffee consumed per day were also recorded. Although all patients had a history of previous treatment with medication, all patients had been hospitalized and medication free for at least 14 days before being admitted to the study. This 2-week medication-free period is considered long enough to negate any effect of medication on the assays.

The 23 comparison subjects were medically and psychiatrically healthy and were recruited and paid for their participation in the study. Comparison subjects were matched in age (plus or minus 5 years) in a one-to-one fashion and sex (all were men) to the patients, were not admitted to the hospital, and met RDC criteria for not mentally ill or never mentally ill. The physical health of all comparison subjects was assessed by medical history and CBC. The comparison group may have been more strictly screened then need be, since "normal" subjects used by the immunology laboratories that originally standardized the mitogen stimulation tests were not screened for mental illness.

Because of the interassay variability of the mitogen response assay, each patient was matched to a comparison subject in age (plus or minus 5 years) and studied on the same day as that comparison subject in each assay run. Male subjects exclusively were used because our principal source of patients, a VA medical center, has mostly male patients.

Mononuclear Cell Collection

By standard clinical phlebotomy, 20 ml of venous blood was drawn into heparinized tubes between 8:30 and 10:30 a.m. to control for the variation caused by circadian rhythms of the immune system. Blood was spun to separate the plasma; then the cellular portion remaining was mixed with an equal volume of RPMI 1640, layered into Ficoll-Hypaque density gradient medium, and centrifuged to separate the monocyte layer. These peripheral blood mononuclear cells were suspended in fully supplemented RPMI 1640 with either 20% fetal bovine serum or 20% autoserum at a concentration of 10^6 cells/ml.

Lymphocyte Proliferation Assay

The proliferative response of lymphocytes to mitogen stimulation was measured by using the following standard technique (7, 13) with minor modifications. The peripheral blood mononuclear cells at 10^6 cells/ml were cultured in either 20% heat-inactivated (by heating at 56 °C for 30 minutes) fetal bovine serum or 20% autoserum in 96 well microtiter plates (0.2 ml/well). (In our previous study, an HB103 serum-free-medium system was used.) Concanavalin A (conA) was used at final concentrations of 20, 15, 10, 5, and 1 μg/ml. Based on previous work in our laboratory, this represents two supraoptimal concentrations (20 and 15 μg/ml), two optimal concentrations (10 and 5 μg/ml), and one suboptimal concentration (1 μg/ml) of each mitogen. After 72 hours of incubation, 2 μCi of 3H-thymidine (methyl-3H-thymidine from Amersham) were added to each culture. After 18 hours, cells were harvested onto glass microfiber filters (Whatman 934-AH) with a micro-automated cell harvester, then scintillated and counted with a Beckman scintillation counter. The results were expressed as the mean of triplicate cultures of the counts per minute of 3H-thymidine incorporated, by using the change in counts per minute (the counts per minute of stimulated experimental wells minus the counts per minute of unstimulated control wells) and also by using the stimulation index (the counts per minute of the stimulated experimental wells divided by the counts per minute of the unstimulated control wells). The data were analyzed twice, by using each method of expression once. If different results were obtained, we explicitly state these results. The rationale for applying both methods of analysis is explained in the Discussion.

We chose conA as the particular mitogen for study because it is the T cell mitogen that has given the better discrimination of patient and comparison groups in our previous work. Phytohemagglutinin (PHA) seemed to have slightly (although not significantly) less utility in this regard. Although T cell dependent, poke weed mitogen is a B cell mitogen. Most studies of immunity in clinical depression and stress have examined and found defects in cellular (T-cell-mediated) immunity rather than humoral (B-cell-mediated) immunity.

Statistical Analysis

For the replication of our previous study (7), the 46 new subjects (23 patients and 23 age- and sex-matched comparison subjects) were used in the analyses. The analyses of all subjects included 86 individuals: patients (N=43) and comparison subjects (N=43). For all analyses, a value of $p<0.05$ was considered significant. Data are occasionally missing for some patients, but not enough to affect the results. Differences in degrees of freedom reflect these missing data.

An analysis of variance (ANOVA) with a repeated measures design (14) was used to test for significance of overall dose-response curve assay results. This analysis was followed by matched t tests for differences in resonse at individual conA concentrations. The analysis was done with the data expressed as change in counts per minute and as stimulation index.

The data from the subjects of the previous study (7) and the present replication were combined, and matched pairs of subjects were divided into two groups according to the relative proliferative response of the patient and his matched comparison subject. One group consisted of subject pairs in which the comparison subject had a higher response than the patient (group A), and the other consisted of pairs in which the comparison subject had a lower response than the patient (group B). Simply put, group A patients fit the hypothesis of lessened immune response in depression, and group B patients responded better (i.e., had a higher lymphocyte proliferation) than their matched comparison subjects. Relative mitogen response was determined by comparing the arithmetic mean of the mitogen response across the range of mitogen concentrations. Patient/comparison subject pairs in which the patient and the matched comparison subject had proliferative responses within 20% of each other were considered to have similar responses and were excluded from the analyses. This method of subject categorization resulted in 16 patient/comparison subject pairs in group A, 15 pairs in group B, and 12 pairs excluded.

We used t tests to determine any difference between patients in group A and group B on relevant continuous variables, and the Mann-Whitney statistic (14) was used for between-group differences on the categorical variables (items from the SADS interview). A stepwise discriminant analysis (14) was used to evaluate the utility of variables for discriminating group A from group B patients. Following this step, a cluster analysis (14) was applied to the variables to determine if some subsets of the subjects could be clustered together based on the data rather than our initial grouping. Finally, to allow better comparison of our results with the results of others (6), parametric correlations were done between age, Hamilton depression scale scores, Beck inventory scores, and each concentration of mitogen in each type of serum, calculated both as change in counts per minute and stimulation index, for all patients, for group A patients, and for group B patients. For the group of all comparison subjects, only age was examined, since the range of Hamilton depression scale and Beck inventory scores in comparison subjects was narrow (0 to 2). Correction of significance for multiple comparisons was not done.

RESULTS

Replication of Previous Study

In the current study, the 23 patients ranged in age from 22 to 71 years, and the 23 comparison subjects ranged from 25 to 68 years. The one-to-one age matching (plus or minus 5 years) produced two groups of subjects that were statistically similar in mean±SD age (patients, 47±13 years; comparison subjects, 48±12 years ($t=0.90$, $df=20$, $p=0.03$, n.s.). The groups had significantly different Hamilton depression scale and Beck inventory scores. For the Hamilton depression scale, the patients' mean±SD score was 18±7 and that of the comparison subjects was 1±1 ($t=-9.70$, $df=16$, $p<0.00009$). For the Beck inventory, the patients' score was 19±8 and the comparison subjects' score was 1±1 ($t=9.18$, $df=15$, $p<0.00009$).

Dose-response curves for both types of serum supplementation (fetal bovine and autoserum) and with the data expressed in both change in counts per minute and stimulation index were calculated by using ANOVA with a repeated measures design. For each of the four conditions there was no significant effect of diagnosis ($0.5<p<0.9$) and no significant diagnosis by dose interaction ($0.4<p<0.9$), meaning that the two groups do not respond significantly differently across the different doses of mitogen. There was a significant

TABLE 1. Results of Matched t Test Analyses of Assays of Lymphocyte Proliferation Performed in Media Supplemented With Fetal Bovine Serum in 23 Depressed Patients and 23 Comparison Subjects

Dose of ConA (μg/ml)	Change in Counts per Minute[a]							Stimulation Index[b]						
	Patients		Comparison Subjects					Patients		Comparison Subjects				
	Mean	SD	Mean	SD	t	df	p	Mean	SD	Mean	SD	t	df	p
1	4.14	0.51	4.31	0.46	0.87	7	0.4	8.5	9.2	8.4	7.7	−0.02	10	0.9
5	4.25	0.79	4.46	0.71	2.14	10	0.06	14.1	14.8	20.4	22.9	0.17	10	0.5
10	4.50	0.63	4.76	0.48	2.11	10	0.06	22.3	26.1	28.8	22.8	0.55	10	0.6
15	4.54	0.77	4.76	0.55	−1.95	10	0.08	30.5	41.1	29.9	23.9	−0.04	10	0.9
20	4.68	0.51	4.72	0.54	0.29	6	0.7	23.2	35.8	26.7	27.2	0.19	6	0.9

[a] Tritiated thymidine incorporation expressed as the log of the counts per minute of stimulated experimental wells minus the counts per minute of unstimulated control wells.

[b] Tritiated thymidine incorporation expressed as the counts per minute of stimulated experimental wells divided by the counts per minute of unstimulated control wells.

TABLE 2. Results of Matched t Test Analyses of Assays of Lymphocyte Proliferation Performed in Media Supplemented With Autoserum in 23 Depressed Patients and 23 Comparison Subjects

Dose of ConA (μg/ml)	Change in Counts per Minute[a]							Stimulation Index[b]						
	Patients		Comparison Subjects					Patients		Comparison Subjects				
	Mean	SD	Mean	SD	t	df	p	Mean	SD	Mean	SD	t	df	p
1	4.01	0.81	4.10	0.81	0.06	19	0.5	35.9	65.2	38.7	50.1	0.18	20	0.3
5	4.56	0.55	4.70	0.56	1.54	20	0.1	71.8	68.4	89.9	82.2	0.95	20	0.4
10	4.68	0.51	4.75	0.55	0.78	20	0.4	102.3	110.0	99.1	86.7	−0.12	20	0.4
15	4.70	0.35	4.76	0.45	0.62	12	0.5	85.1	73.9	95.6	97.1	0.45	12	0.7
20	4.65	0.32	4.80	0.43	1.34	8	0.2	73.1	69.1	90.6	99.3	0.73	8	0.5

[a] Tritiated thymidine incorporation expressed as the log of the counts per minute of stimulated experimental wells minus the counts per minute of unstimulated control wells.

[b] Tritiated thymidine incorporation expressed as the counts per minute of stimulated experimental wells divided by the counts per minute of unstimulated control wells.

effect of dose for each of the four conditions, as expected ($4.15 \leq F \leq 19.57$; df=3, 54; 4, 52; 3, 33; 3, 36; $0.00009 < p \leq 0.0054$).

In addition to the overall effect as expressed in a dose-response curve, we were interested in whether the two groups would be significantly different at any single dose. We tested this question by using matched t tests. For the assays of lymphocyte proliferation performed in media supplemented with fetal bovine serum with the data expressed as change in counts per minute, there was a strong trend for the comparison subjects to have more proliferation than the patients at the supraoptimal dose of 15 μg/ml and the optimal doses of 10 and 5 μg/ml (see table 1). At the suboptimal and supraoptimal doses of 1 and 20 μg/ml, no significant differences were found between groups, nor were there any significant differences between groups at any of the five doses for fetal bovine serum when the data were expressed as stimulation index (see table 1).

For the assays of lymphocyte proliferation performed in media supplemented with the autoserum, there was no significant difference between groups at any of the five doses of conA, whether the data were expressed as change in counts per minute or as stimulation index (see table 2).

New Analysis of Subjects From Both Studies

A t test was done between the 16 patients in group A (those with lower responses than their comparison subjects in this study and the previous study [7]) and the 15 patients in group B (those with higher responses than their comparison subjects in this study and the previous study). The variables examined were age, educational level, Hamilton depression scale score, Beck inventory score, BPRS depression subscale score, BPRS anergia subscale score, BPRS total score, cigarette use, and coffee use. Age, number of years of education, packs of cigarettes smoked per day, cups of coffee consumed per day, Hamilton depression scale scores, and Beck inventory scores were similar in the two groups (see table 3). A significant difference between the two groups existed for BPRS depression subscale score, BPRS anergia subscale score, and total BPRS score (see table 3). Note that the group A patients, who had lower proliferative responses than their matched comparison subjects, had lower BPRS depression subscale scores, BPRS anergia subscale scores, and total BPRS scores than the group B patients.

Individual items from the SADS interview (somatic anxiety, psychic anxiety, obsessions and compulsions, insomnia, agitation, and psychomotor retardation)

TABLE 3. Demographic and Clinical Characteristics of the Depressed Patients in 31 Pairs of Depressed Patients and Comparison Subjects Grouped According to Comparative Lymphocyte Proliferative Responses

Item	Group A[a]		Group B[b]				
	Mean	SD	Mean	SD	t	df	p
Age (years)	46	13	45	12	−0.14	28	0.9
Number of years of education	13	2	13	2	−0.09	24	0.9
Hamilton depression scale score	19	7	25	11	1.67	29	0.1
Beck Depression Inventory score	22	10	22	10	−0.27	27	0.8
BPRS depression subscale score	10	3	14	4	2.57	22	0.02
BPRS anergia subscale score	6.0	2.1	9.4	3.5	2.93	22	0.008
BPRS total score	43	10	54	13	2.46	22	0.02
Number of packs of cigarettes smoked per day	1.4	0.8	0.8	0.9	−1.62	20	0.1
Number of cups of coffee consumed per day	3.7	2.9	2.3	1.6	−1.43	21	0.2
Somatic anxiety[c]	3.0	1.1	2.8	1.6	92.0[d]	—	0.8
Psychic anxiety[c]	2.7	1.5	3.4	1.3	132.0[d]	—	0.2
Obsessions and compulsions[c]	1.3	0.8	2.4	1.6	147.5[d]	—	0.03
Insomnia[c]	3.9	1.6	4.4	1.2	114.5[d]	—	0.4
Agitation[c]	2.5	1.4	2.7	1.2	117.5[d]	—	0.6
Psychomotor retardation[c]	2.2	1.0	3.3	1.4	151.5[d]	—	0.04

[a] The depressed patients had lower lymphocyte proliferative responses than their matched comparison subjects.
[b] The depressed patients had higher lymphocyte proliferative responses than their matched comparison subjects.
[c] According to SADS interview.
[d] Mann-Whitney statistic.

were used in between-group analyses to help characterize the depression of the patients in group A versus group B. Since these are categorical variables, the Mann-Whitney statistic was used. A significant difference was found between the two groups for obsessions and compulsions and psychomotor retardation (see table 3): the group A patients had fewer obsessions and compulsions and less psychomotor retardation than the group B patients. The two groups did not differ in the other SADS item variables examined (somatic anxiety, psychic anxiety, insomnia, and agitation) (see table 3).

Next, a stepwise discriminant analysis was applied by using the continuous variables found to be different between the two groups to evaluate the utility of these variables for discriminating whether a patient with major depression had better or worse lymphocyte proliferation than his matched comparison subject. The subject pairs in group A were correctly classified in 69.2% of the cases, in group B in 63.6% of the cases, and overall in 66.7% of the cases.

The subjects were next grouped by cluster analysis into two clusters. One contained ten group A patients and five group B patients (67% correct clustering of group A subjects), and the other cluster contained five group A patients and nine group B patients (64% correct clustering of group B subjects). The BPRS depression subscale score contributed most strongly to this clustering ($F=20.45$, $df=1, 22$, $p<0.0009$), followed in order of strength of contribution by the Beck inventory score ($F=19.37$, $df=1, 27$, $p<0.0009$), BPRS total score ($F=12.29$, $df=1, 22$, $p=0.002$), Hamilton depression scale score ($F=11.74$, $df=1, 27$, $p<0.002$), and BPRS anergia subscale score ($F=8.61$, $df=1, 22$, $p=0.008$). The other variables used did not significantly contribute to the cluster sorting.

Finally, on parametric correlational analysis among 37 of all 43 patients, higher age correlated significantly with lower lymphocyte proliferation (conA=5 μg/ml, autoserum supplementation, expressed as change in counts per minute, $r=-0.33$, $df=36$, $p=0.043$). Among the 10 patients who received suboptimal doses of conA and who also had Hamilton scores, a higher Hamilton depression scale score correlated significantly with lower lymphocyte proliferation (conA=20 μg/ml, autoserum, expressed as stimulation index, $r=-0.62$, $df=9$, $p=0.042$). For the group A patients only, higher age correlated significantly with lower lymphocyte proliferation (conA=5 μg/ml, autoserum, stimulation index, $r=-0.49$, $df=15$, $p=0.045$). For the 15 patients in group B only, there were no significant correlations between the variables examined. Among 30 of all 43 comparison subjects, however, higher age correlated significantly with lower lymphocyte proliferation (conA=10 μg/ml, autoserum, change in counts per minute, $r=-0.37$, $df=29$, $p=0.041$; conA=10 μg/ml, autoserum, stimulation index, $r=-0.36$, $df=29$, $p=0.046$).

DISCUSSION

According to the findings of the present study, BPRS depression subscale score, BPRS anergia subscale score, total BPRS score, SADS obsessions and compulsions, and SADS psychomotor retardation may represent measures of augmentation or mitigation of the effect of mood state on mitogen-induced lymphocyte proliferation. However, given the unexpected direction of these data (the less depressed, less anergic, less retarded patients with lower total BPRS scores and fewer obsessions and compulsions had lower proliferative responses), the simplistic view that depressed patients as a group have a poor immune response as measured by mitogen-induced lymphocyte proliferation must be reexamined. This conclusion is strengthened by results from previous studies (1–7) indicating that there does not seem to be a clear and marked difference in in vitro mitogen-induced proliferative response of peripheral blood lymphocytes in all depressed patients when compared with mentally and physically healthy comparison subjects. The discriminant analysis and cluster analysis contributed little to our understanding of the results (correct classification of less than 80% of cases is not considered useful). There may be alternative hypotheses that should be tested. For example, measurable immune change may lag behind the state of depression temporally, or the circadian changes in immune activity may be advanced or retarded.

Another recent major study (6) also found no difference in lymphocyte proliferation between depressed patients and comparison subjects but did report that lymphocyte proliferation was related to age and severity of depression. Our groups, both the patients versus the comparison subjects and group A patients versus group B patients, were closely matched in age, but the patients had no difference in lymphocyte proliferation from the comparison subjects, and the patients in group A and group B had dramatically different lymphocyte proliferative responses than their matched comparison subjects. Similarly, Hamilton depression scale scores and Beck inventory scores of the patients were very different from those of the comparison subjects, although the two groups had similar lymphocyte proliferative responses, and patients in groups A and B were matched on Hamilton depression scale and Beck inventory scores but had markedly different lymphocyte proliferative responses. Although the BPRS depression subscale scores of patients in groups A and B were significantly different, it was the less depressed group A that had the poorer lymphocyte proliferation.

In the present study we found a weak relation between Beck inventory and Hamilton depression scale scores and lymphocyte proliferation: these measures of severity of depression, along with the BPRS depression subscale score, contributed significantly to the two clusters in the cluster analysis. This view is mitigated by the overlap of the clusters (the group A cluster included 67% of the group A patients, and the group B cluster included 64% of the group B patients) and the fact that the Hamilton depression scale score was lower (although not significantly) in group A patients than group B patients.

On correlational analyses, a better case can be made for a relationship between age and lymphocyte proliferation when stimulated by optimal doses (5 or 10 μg/ml) of conA. A weaker case is built for the relationship of objectively rated depression (by using the Hamilton depression scale) in the group of all patients combined, and no significant correlations of subjectively rated depression (by using the Beck inventory) with lymphocyte proliferation were found. Caution in interpretation of these correlations is also necessary because of the large number of correlations tested, which increases the chance that a random few will be significant. Any relationship between age or severity of depression and mitogen-induced lymphocyte proliferation would have to be called inconsistent.

As explained in our previous publication (7), we present and analyze the data expressed in two formats (see Method). Each format has its proponents. Many clinicians feel that the stimulation index is more reliable because it may have a lower interassay coefficient of variation. The stimulation index weighs any proliferation of unstimulated cells more heavily, so that the actual effect of mitogen stimulation is readily noted. Many researchers not using their test results in the clinical care of patients, however, feel that the change in counts per minute more accurately displays the ability of the lymphocytes to proliferate. It may be interesting to repeat this study using PHA and poke weed mitogen. However, we have no evidence that different results would be obtained, and such repetition would require considerable effort and resources.

Previous efforts in this area used various types of medium supplementation for the assay. The initial work used 10% fetal bovine serum (1); others used 20% autologous plasma (2), 40% heat-inactivated horse serum (3, 4, 6), or 5% fetal bovine serum (5). Given the many factors in serum that may confound the investigation of the mechanism of any reduced proliferative response found in depressed patients, our earlier work used the HB103 serum-free medium and culture system (7). On analyzing the data with equivocal results, we returned to serum supplementation and added the autoserum (serum from the same individual as the cells) supplementation along with the fetal bovine serum, both at a moderate percent of the total medium (20%). Tendencies toward differences between the patient and comparison groups for change in counts per minute were found for the bovine-serum-supplemented assays but not for the autoserum-supplemented assays (see tables 1 and 2), and the autoserum stimulation index was generally much higher for all subjects than the fetal bovine serum stimulation index (see tables 1 and 2). In summary, the tests need to be standardized across studies, and comparisons of studies are weakened by differences in the assay.

In another clinical study (15), the mitogen (PHA)-induced proliferative response bore little relationship to immunologic anergy as measured by the delayed hypersensitivity skin test, an in vivo measure of the immune response to antigenic challenge that we are now using to evaluate immunity in depressed patients (16). Yet another study (17) has documented that the mitogen-induced cell proliferation assay has the highest coefficient of variation of any of 16 immune assays tested in 61 healthy individuals, with repeat testing over a 14-month period. There was a lack of high correlations between this assay and any other immune assay. As mitogen-induced proliferation was studied repeatedly in the same individuals over longer periods of time, the percentage of total variability due to interindividual differences shrank to near zero or zero and the intraindividual variability increased. There exist variations in this laboratory assay; there are periods of time when all concentrations of mitogen result in consistently high or low proliferation. The reasons for this variation are unknown but seem to reflect the assay rather than biological significance. Changes in a subject's lymphocyte response measured over long periods of time (greater than 6 months) may primarily reflect variability associated with assay conditions rather than immunologic changes. In the present study we attempted to negate this assay variability over time by running each experimental subject with his age- and sex-matched healthy comparison subject together on the same day.

Another confound introduced by this assay arises from its in vitro nature. The cells are incubated in tissue culture for 96±24 hours (depending on the technique used). During this time they are actively replicating and proliferating outside of the in vivo physiological milieu from which they came. The resulting cells at endpoint may little reflect the physiological environment within stressed or depressed individuals.

The extremely weak correlation between mitogen response and immunological status is well-known among clinical immunologists. Only when the mitogen responses are severely and repeatedly depressed (i.e., stimulation index less than 10 at optimal mitogen concentrations) is there a reasonable association with greater susceptibility to infections (18). At least one worker investigating the effects of stress on the immune system in an animal model (19) has become skeptical of the utility of mitogen-induced lymphocyte proliferation in preclinical research in psychoimmunology. On the other hand, in an unpublished paper, Dr. Christopher Coe, working in a primate model, reported excellent reproducibility of the mitogen response findings but cautioned that longitudinal study with serial monthly determinations of lymphocyte proliferation are needed to obtain this reproducibility. However, published studies by Dr. Coe's group are marred by the same flaws and difficulties of most studies using this assay technique—the use of only one determination or, at times, two determinations separated by more than a year and high individual variation (20, 21). These issues have a wider relevance beyond the field of psychoimmunology. Solid, replicated foundation studies have never been done by medical immunologists to demonstrate the purported link between reduced in vitro proliferation of lymphocytes after polyclonal stimulation by plant lectins and other mitogens and immunosuppression or clinical illness. Such a link, if it exists at all, may be weak.

It is important to note that we are unable to comment on other assays of immune function, such as enumeration of peripheral circulating white cells or natural killer cell activity, or other assays of immune status or function, on the basis of this work.

Given what we have just said, one may wonder why the assay should be used at all. In some clinical situations (e.g., the DiGeorge anomaly) it may be useful in discriminating patients with immunodeficiency (18). Further, new studies in psychoimmunology continue to confirm the original studies' description of lower lymphocyte proliferation in severe depression (22), leaving the literature and scientific understanding of the phenomenon (if there is one) in conflict. It may be that studies with fewer subjects are completed during a shorter period of time, with less laboratory assay drift. Results from such studies may therefore more accurately depict lower immune cell function in depression than do larger studies. It would be most helpful and satisfying to have firm answers. Additionally, in research settings the assay may have utility in investigating the mechanism of any immune alterations consistently found in a given paradigm. For example, if conA-induced cell activation (as measured by intracellular calcium flux over 1–2 minutes) were done in conjunction with the 3–4-day conA-induced lymphocyte proliferation assay, with repeated measures of the experimental subjects over time (or replicate experiments in rodent models with genetically similar individuals), our information about the cells' ability to function may be greatly enhanced. Similarly, if purified T or B cells or cell subsets were evaluated in such an assay system, it would sharpen our ability to dissect the mechanisms involved. Another approach would be to plan studies to measure possible serum-borne immune mediators affecting lymphocyte proliferation (e.g., interleukin-1, interleukin-2, or β-endorphin) in addition to the proliferative response itself.

If we assume the assay has continued value, there may be three methods to reduce the variance, in addition to the pairing of experimental and comparison subjects on each assay day. One method, modeled after Dr. Coe's concept, would be to design any study of mitogen-induced lymphocyte proliferation to be a longitudinal study with daily, weekly, or monthly repeated measures (depending on the rapidity of change of the clinical or experimental situation) in the same subjects. This design would obtain a better measure of the baseline ability across time of the individual subject's lymphocytes to proliferate when stimulated and would allow each subject to serve as his own "control" to determine whether he or she on average had low, moderate, or high lymphocyte proliferative responses to mitogen. The least acceptable frequency would probably be monthly to bimonthly, to allow investigators to gage and correct for the drift of the assay in their laboratory over time. This point about longitudinal study cannot be emphasized enough.

The second technique involves running a constant lymphocyte population in each assay run. Lymphocytes are drawn from a carefully screened, mentally and physically healthy comparison subject in one large phlebotomy, separated, stored on liquid nitrogen, and thawed for each assay run. This method may be less necessary in rodent models with genetically similar individuals but is easily accomplished by using the total blood volume or splenic lymphocyte population from several animals, pooled, processed, and stored. This technique may allow stabilization of the inevitable and unexplained variation of this assay over time in each laboratory where it is used, with experimental and comparison subject proliferation expressed as a percentage of the proliferative response of the constant lymphocytes. We are currently evaluating both of these methods of assay stabilization in our laboratories.

The third technique would be to separate the lymphocytes from experimental subjects and store the cells on liquid nitrogen. Then, at the experiment's conclusion, thaw and assay all cell samples within a brief (less than 6 months) time interval. Where practical (which, unfortunately, is seldom), experiments should be designed so that they can be completed within 6 months of initiation, minimizing the effect of assay drift.

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12-Month Outcome of Patients With Major Depression and Comorbid Psychiatric or Medical Illness (Compound Depression)

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Objective: Inpatients with major depressive illness often have coexistent nonaffective psychiatric and/or medical conditions. The authors' objective is to address the following questions: 1) What is the effect of comorbid illness on the severity of major depression and associated psychosocial factors? 2) How does the course of depression differ for patients with and without concurrent illness? 3) Do patients with compound depression differ in rate of recovery and time to recovery from patients with pure depression? Method: The subjects were 78 patients with a DSM-III *diagnosis of major depression who were consecutively admitted to an acute care university-affiliated psychiatric hospital; 37 of these patients had major depression only and 41 had major depression compounded by a coexisting axis I, II, or III condition. The patients were studied while hospitalized and for 12 months after hospital discharge. Instruments used included the Modified Hamilton Rating Scale for Depression, the Global Assessment Scale, and the Social Readjustment Rating Scale. Results: Patients with compound depression reported significantly poorer functioning over the 12-month follow-up period and had lower recovery rates than the patients with pure depression. There were no differences in recovery rates between men and women with compound depression, but significantly more men than women with pure depression recovered. Conclusions: Compound depression is a common clinical occurrence, the course of illness is more difficult for patients with compound depression than for patients with pure depression, and the recovery rate of patients with compound depression is lower than that of patients with pure depression.*

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Up to one-half of inpatients diagnosed as having major depressive illness have a coexistent nonaffective psychiatric and/or medical condition (1–4). Because of the frequency with which comorbidity occurs, it is clinically important to understand how concurrent illness affects the course, treatment, and outcome of a major depressive episode. Using the primary-secondary framework of Robins and Guze (5), several studies have focused on comorbidity in patients with major depression. Overall, the results of these studies have been suggestive but inconclusive, mainly because of varying ways of categorizing the comorbid conditions.

Similarities in acute symptoms, severity of the depressive illness, psychoticism, and treatment received have been reported for depressed patients with and without other illnesses. Reports of differences include an earlier age at onset of the depressive illness, longer duration of the depressive episode, and higher rates of family history of alcoholism and personality disorders for patients with secondary depression compared with patients with primary depression (1, 3, 6–10). Although Clayton and Lewis (3) found no differences between patients with primary and secondary depression in suicidal behavior, others (7, 10) have found that comorbidity was associated with more previous suicide attempts and more suicide ideation.

In contrast to the acute stage of the illness, there appears to be more consensus when comparisons are made over the course of depressive episodes and in the patients' outcome. Andreasen and Winokur (1) and

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Hirschfeld et al. (11) found no significant differences in recovery rates between depressed patients with and without coexisting diagnoses. Most studies (3, 7–10, 12–14), however, reported poorer recovery rates and/or response to treatment at discharge or 6-month follow-up for patients with depression and comorbid illness.

Interestingly, a poorer outcome and response to treatment characterize depressed patients with concurrent illness irrespective of the coexisting diagnosis (3, 7–10, 12–14). These studies suggested that any additional burden, rather than the burden caused by a specific illness, is the determining factor in predicting a poorer prognosis. One way to further explore this question of the effect of specific illnesses is to study large numbers of patients with a variety of comorbid conditions.

Another approach is to group coexistent conditions together without a priori assumptions about the specific effect of any particular concurrent illness. We did so in order to test whether the presence of any additional psychiatric, personality, or medical disorder would adversely affect the course and outcome of a major depressive episode. Patients with major depression only (patients with pure depression) were compared with patients with major depression plus an additional axis I, axis II, or axis III disorder (patients with compound depression). We used the term "compound depression" as opposed to the primary-secondary dichotomy of Robins and Guze (5) to avoid assuming a causal ordering of the coexisting conditions (15).

Comparisons were made between patients with pure and compound depression at the acute stage of depressive illness (during hospitalization) as well as over a 12-month follow-up period after hospital discharge. This was a naturalistic prospective study that addressed the following questions: 1) What is the effect of comorbid illness on the severity of major depression and associated psychosocial factors? 2) How does the course of depression differ for patients with and without concurrent illness? 3) Do patients with compound depression differ in the rate of recovery and time to recovery from patients with pure depression?

METHOD

The subjects for the study were 78 patients consecutively admitted to an acute care university-affiliated psychiatric hospital who had *DSM-III* diagnoses of major depression and who lived with at least one other family member over the age of 12 years. The patients' admission diagnoses of major depression were confirmed independently by chart review by two clinicians as well as by administering the affective disorders section of the National Institute of Mental Health Diagnostic Interview Schedule (16).

The group studied included 37 patients with major depression only (patients with pure depression) and 41 patients with major depression compounded by a coexisting psychiatric and/or medical condition (patients with compound depression).

The mean±SD ages of the patients with pure and compound depression were 42.2±11.6 and 41.8±15.1 years, respectively. The proportions of male to female patients in the groups of patients with pure and compound depression were 0.42:1 and 0.71:1, respectively. There were no significant differences between the patients with pure depression and the patients with compound depression on these or other sociodemographic variables, including marital status, number of years married, number of children, number of years of education, or socioeconomic status (14).

By the final follow-up at 12 months after hospital discharge, four of the patients with pure depression and seven of the patients with compound depression had dropped out of the study. Complete data for the entire follow-up period were collected for the remaining 67 patients (86% of the original study group). Partial information was available and used when appropriate for three of the patients who dropped out of the study (one patient with pure depression and two patients with compound depression).

Information collected during hospitalization included sociodemographic data as well as psychosocial and clinical measures of depressive symptoms, age at onset of depression, suicidality, severity of depression, family history of psychiatric illness, and family composition.

Patients were given the 17-item Modified Hamilton Rating Scale for Depression (17) to monitor the severity of their depressive illness over time at three family meetings (during hospitalization, at 6-month follow-up, and at 12-month follow-up) as well as during monthly telephone interviews.

The Global Assessment Scale (18) was administered on a monthly basis to evaluate patients' overall functioning on a continuum ranging from psychological illness to health.

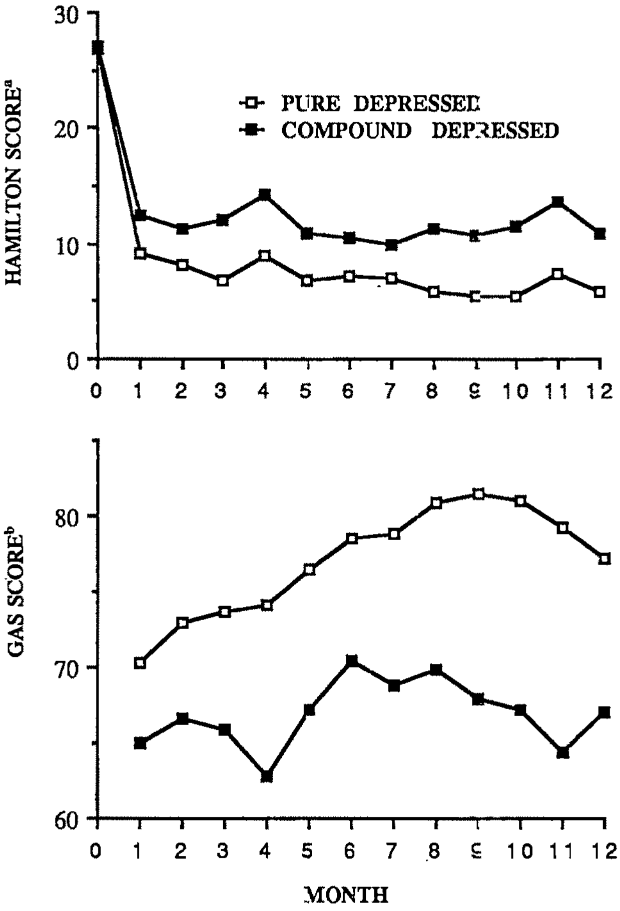
The Social Readjustment Rating Scale (19) was completed by an adult family member at the 6- and 12-month follow-up meetings. This scale is a checklist of 40 possible life events, including such items as divorce, job loss or promotion, and change in living conditions. Any event that occurred within the previous 6 months was reported; absolute totals and weighted scores were analyzed.

The findings presented here focus on the 12-month outcome and course of illness for patients with pure depression compared with patients with compound depression. Recovery was defined as a Hamilton scale score of less than 7 for 3 consecutive months; relapse was defined as a Hamilton scale score of 18 or greater after a patient had recovered. Life table techniques were used to generate the percent of patients recovered over the 12-month study period. Relationships between categorical variables were tested for significance by using chi-square analyses; t tests and analyses of variance were used to test for differences of continuous measures.

TABLE 1. Comorbid Diagnoses of 41 Patients With Depression Plus Another Axis I, II, or III Disorder

Comorbid Diagnosis	Number of Patients
Axis I	17
Dysthymic disorder	4
Substance abuse	4
Anxiety disorder	5
Bulimia	1
Obsessive-compulsive disorder	3
Axis II	8
Avoidant or dependent personality disorder	3
Histrionic or narcissistic personality disorder	2
Schizotypal personality disorder	1
More than one diagnosis	2
Axis III	8
Cardiovascular disorder	4
Diabetes	1
Epilepsy	1
Asthma	1
Chronic pain	1
Combination of axis I, II, and III disorders	8

FIGURE 1. Severity of Depression and Overall Functioning Over a 12-Month Period After Hospital Discharge of 37 Patients With Pure Depression and 41 Patients With Compound Depression



[a] Severity of depression was measured by scores on the Modified Hamilton Rating Scale for Depression. The groups were significantly different from each other at 3 months (t=2.55, df=69, p<0.02), 4 months (t=2.07, df=72, p<0.05), 8 months (t=2.38, df=65, p<0.02), 9 months (t=2.74, df=66, p<0.01), 10 months (t=2.60, df=63, p<0.02), 11 months (t=2.15, df=63, p<0.05), and 12 months (t=2.43, df=63, p<0.02).

[b] Overall functioning was measured by scores on the Global Assessment Scale. The groups were significantly different from each other at 3 months (t=2.13, df=73, p<0.05), 4 months (t=2.67, df=71, p<0.01), 5 months (t=2.41, df=71, p<0.02), 7 months (t=2.32, df=68, p<0.05), 8 months (t=2.74, df=65, p<0.01), 9 months (t=3.15, df=66, p<0.01), 10 months (t=2.89, df=63, p<0.01), 11 months (t=2.95, df=63, p<0.01), and 12 months (t=2.04, df=60, p<0.05).

RESULTS

The 41 patients with compound depression represented more than half (53%) of the 78 depressed patients. The coexisting disorders fell into a wide range of categories; no one type of illness predominated (see table 1).

During the acute phase of the depressive episode the patients with pure and compound depression did not differ from each other on most clinical and psychosocial variables (14). Some differences emerged, however, over the course of the illness.

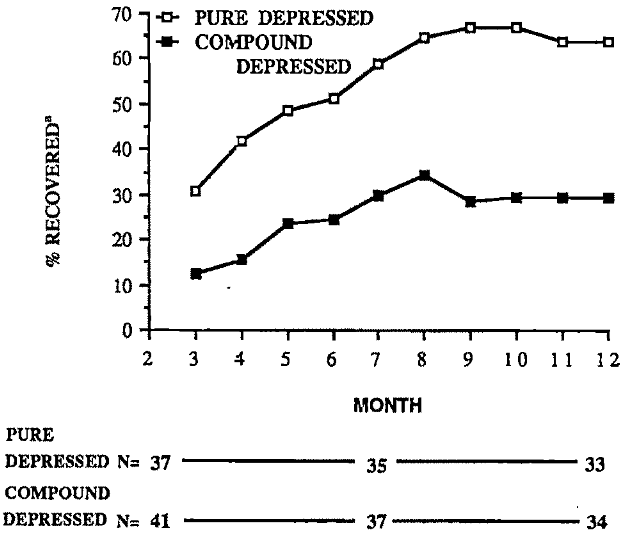
Figure 1 shows the severity of depressive symptoms in the patients with pure and compound depression over the 12-month study period. There was a dramatic drop in severity scores for both groups as early as 1 month after hospital discharge. Even though a gap in symptom severity between the two groups was immediately apparent, the difference did not attain significance until the third month after hospital discharge. From the eighth month onward this difference became consistently significant.

The pattern of overall adjustment of depressed patients, also shown in figure 1, parallels that found for depressive symptoms. As in the ratings of symptom severity, the third month marked the first point at which patients with pure depression showed significantly better global adjustment than patients with compound depression. After this, with the exception of the sixth month, patients with pure depression scored significantly better in their overall functioning than did patients with compound depression.

In our previous report (14), we noted that 51% (N=18) of the patients with pure depression had recovered by the 6-month follow-up period, compared with 28% (N=11) of the patients with compound depression. At 12 months, the recovery rates were even more divergent: 65% (N=22) of the 34 patients with pure depression remaining in the study versus only 33% (N=12) of the 36 remaining patients with compound depression (χ^2=6.79, df=1, p<0.01).

In fact, throughout the follow-up period, roughly half as many patients with compound depression as patients with pure depression recovered (see figure 2). Furthermore, there were no significant differences in recovery rates among the patients with compound depression.

FIGURE 2. Percent of 37 Patients With Pure Depression and 41 Patients With Compound Depression Who Recovered Over a 12-Month Period After Hospital Discharge



[a] The groups were significantly different from each other at 4 months ($\chi^2=6.33$, df=1, $p<0.02$), 5 months ($\chi^2=4.85$, df=1, $p<0.05$), 6 months ($\chi^2=5.56$, df=1, $p<0.02$), 7 months ($\chi^2=6.01$, df=1, $p<0.02$), 8 months ($\chi^2=6.29$, df=1, $p<0.02$), 9 months ($\chi^2=9.75$, df=1, $p<0.01$), 10 months ($\chi^2=9.18$, df=1, $p<0.01$), 11 months ($\chi^2=7.77$, df=1, $p<0.01$), and 12 months ($\chi^2=7.77$, df=1, $p<0.01$).

As figure 2 illustrates, recovery rates for patients with pure and compound depression showed steady improvement through the eighth month of follow-up and then declined (due to relapse) or reached a plateau. Most of the patients who recovered did so within 6 months of hospital discharge; two patients with pure depression and four with compound depression relapsed by month 12.

Although this study was naturalistic in design, we did examine the types of treatment received by each group of depressed patients. Although they had lower rates of recovery than patients with pure depression, significantly more of the patients with compound depression received individual therapy after hospital discharge (94% [N=31] versus 64% [N=21], $\chi^2=9.07$, df=1, $p<0.01$). There was no difference in the percentage of patients in each group who received family therapy or group therapy or in the duration of treatment received by the patients in each group.

On discharge from the hospital, most patients received some type of pharmacotherapy: 84% (N=31) of the patients with pure depression and 88% (N=36) of the patients with compound depression continued to receive medication for their depression. At the 12-month follow-up, 61% (N=20) of the 33 patients with pure depression who remained in the study reported that they were still taking medication, compared with 48% (N=16) of the 33 patients with compound depression who remained in the study ($\chi^2=0.963$, df=1, n.s.). We were unable to collect further systematic data on levels of pharmacotherapy received by either group of patients.

An interaction effect on recovery rates was found between pure versus compound depression and gender. Although there were no differences in recovery rates for men and women among the patients with compound depression, there was a strong relationship between gender and recovery status among the patients with pure depression. By the 12-month follow-up, significantly more men (100% [10 of 10]) than women (50% [12 of 24]) with pure depression had recovered ($\chi^2=7.17$, df=1, $p<0.01$).

We found no relationship between number of life events reported and pure versus compound depression. Patients with pure depression had a mean of 4.5 reported life events, and the patients with compound depression had a mean of 5.4 (t=0.778, df=46, n.s.). However, in both groups of patients, those who did not recover reported that they experienced significantly more events than did patients who recovered—6.7 versus 2.9 (for patients with pure depression, t=2.86, df=22, $p<0.01$; for patients with compound depression, t=2.11, df=22, $p<0.05$). Although the mean scores within the group of patients with pure depression and within the group of patients with compound depression were identical, the levels of significance for the difference in mean scores between those who did and did not recover differed between groups.

No differences were found between groups when events were classified as positive or negative in nature, family-related, job-related, or associated with psychological loss. Thus, although the number of events was significantly related to recovery status, we were unable to discover any particular class of event that affected outcome.

DISCUSSION AND CONCLUSIONS

The overall goal of this study was to assess the impact of comorbidity on the course and outcome of depressive illness. Three conclusions are evident from the study. First, compound depression appears to be a common clinical occurrence in inpatient psychiatric settings. Second, the course of illness for patients with compound depression is more difficult than for patients with pure depression. Third, recovery rates in patients with compound depression are significantly lower than those for patients with pure depression.

Even though no attempt was made to select for patients with concurrent illness, more than half of the depressed patients in this study had a coexistent disorder. Further, the additional disorder was not limited to a particular *DSM-III* axis or, within each axis, to any particular cluster of disorders. We know that major depression is heterogeneous in nature, so perhaps it should not be surprising that associated comorbidity is heterogeneous as well.

Whatever the coexisting diagnosis, it seems clear that patients with compound depression have a poorer course of illness than do patients with pure depression. By the third month after hospital discharge, the patients with pure depression had significantly better scores for overall functioning than did the patients with compound depression. This finding is consistent with research comparing depressed patients with and without axis I or axis II disorders (8, 11, 13) and with more recent studies suggesting a similar course for those with axis III disorders (20–22). It appears that it is not the coexistence of a specific type of illness but any illness that is associated with a more difficult course of depression.

Not only did patients with pure depression have significantly better scores for overall functioning than did patients with compound depression, twice as many patients with pure depression recovered. Although levels of recovery differed dramatically between patients with pure and compound depression, recovery from the depressive episode was likely to occur within 6 months after hospital discharge for any patient who recovered. This time frame is similar to that reported in the literature (11, 23, 24). Importantly, however, we found that differences between patients with pure and compound depression were sustained over time: the patients with compound depression continued to experience lower recovery rates and generally required more intensive ongoing care.

We found no significant difference in recovery rates within the group of patients with compound depression when grouped by concurrent axis I, II, or III disorders or a combination of these disorders. It may be that the presence of any additional psychiatric or medical condition will prolong the course of the depressive episode and reduce the prospects of recovery.

Several explanations could account for the poor recovery rates of patients with compound depression. Inadequate treatment or noncompliance in taking medications are two obvious possibilities. There were, however, no significant differences between patients with pure and compound depression in in-hospital pharmacotherapy or in the percentages of patients reporting taking medications at 12 months.

Similar proportions of patients with pure and compound depression received group therapy, family therapy, and medication management after leaving the hospital. Significant differences were apparent only for individual therapy. There was no difference in the length of time in treatment, however; both groups averaged 8½ months. Therefore, in spite of the fact that a greater percentage of patients with compound depression received psychotherapy, they still had a worse outcome. Either the type of psychotherapy they were given was not particularly helpful or, more likely, their illnesses were more impervious to standard treatments.

Alternative explanations for differences in recovery rates might also be found in the nature of compound depression. A patient with compound depression may not be able to respond to treatment in the same way a patient with pure depression can. Further, if short-term hospitalization and treatment for the depression alone is stressed, then other problems may not be addressed properly, thereby prolonging the time to full recovery. Finally, the effect of hospitalization as a respite may last for a shorter length of time for patients with multiple problems.

An interesting and unexpected finding was the interaction of gender and whether the depression was compound or pure and recovery status. Although men and women in the group of patients with compound depression did not differ in recovery rates, significantly more men than women with pure depression recovered.

Several studies (24, 25) have reported trends toward higher recovery rates and fewer relapses for males than for females. Frank et al. (26) found no significant gender differences in recovery rates at 16-week follow-up, even though males were better responders; these authors suggested that sex differences in the outcome of depression may become more pronounced over time. Few reports, however, have specifically addressed comorbidity and gender difference in recovery rates (27).

Sex differences in recovery rates may be related to the social roles of men and women (28) or may be due to biological differences in depressive illness between men and women (29). We found no evidence of sex differences in severity of illness; furthermore, we are not aware of any studies that support a neurobiological explanation for gender differences in recovery rates. For patients with compound depression, the greater burden of the concurrent illness may override any differences in outcome between men and women.

Finally, our finding that, within each depressed group, the patients who recovered reported fewer life events than did those who did not recover has received some support from other studies (21, 30). We found no common basis to classify the events reported. It may be that the number of events rather than the nature of events can impede progress toward recovery.

In conclusion, this study stresses the importance of identifying and dealing with the implications of comorbidity in patients with major depression. The lower recovery rates and prolonged morbidity of patients with compound depression present a clinical challenge and an economic burden. Continuing research is needed to further address key issues, such as the probability of recurrence of the depression, the length of the depressive episode, long-term prognosis, and the effectiveness of various treatment approaches.

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Depressive Symptoms Following Stroke

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Objective: The primary purpose of this study was to assess the relation of lesion location to mood and vegetative disturbance following stroke. Method: Fifty-two inpatients and outpatients who had had single, unilateral strokes were included. Patients with past CNS or psychiatric disorders were excluded. A modified Visual Analogue Dysphoria Scale was used to allow the inclusion of all but the most impaired aphasic patients. Sleep and eating disturbances were measured by using both self-report and nursing assessments. Location of lesions was determined by CT scan and classified according to three dimensions: right-left, dorsal-ventral, and frontal-nonfrontal. Results: On measures of dysphoric mood and sleep disturbance, results indicated significant three-way interactions among the three lesion dimensions. No differences were found with regard to eating disturbance. Greater dysphoria and sleep disturbance were found in subjects with left parietal/occipital, left inferior frontal, right superior frontal, and right temporal lesions than in subjects with lesions in other locations. Depressive symptoms were not associated with functional impairment as measured by activities of daily living, motor strength, or severity of aphasia. Conclusions: These results support the hypothesis that lesion location is a valid and significant factor in the mixture of influences which may result in a dysphoric mood state following stroke. The relation between the site of the lesion and subsequent depressive symptoms, however, may be more complex than has been reported previously.

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Mood disorders following stroke are common (1), can significantly reduce the speed and success of rehabilitation (2), and do not appear merely to represent an expected grief response to loss of function (3, 4). Robinson and colleagues (5, 6) suggested that patients with left anterior cerebral lesions have a higher incidence and severity of the psychiatric syndrome of major depression than do patients with lesions in other locations. A more recent report by Robinson's group (7) and one by others (4), however, indicate that this finding may not be as definite as was first thought.

A more precise assessment of intrahemispheric lesion location may help to clarify the relation between lesion focus and depressive symptoms. On the basis of known neuroanatomical connections of cortical/subcortical limbic system pathways, it would be expected that differences in mood and behavior would exist within frontal or posterior regions, depending on whether a lesion is in a more ventral or dorsal location (e.g., orbital frontal versus dorsolateral frontal lobe or temporal versus parietal lobe) (8–10). Despite the existence of these dorsal-ventral neuroanatomical differences, no previous study of poststroke mood disorders has systematically evaluated this aspect of lesion localization.

A major limitation to previous investigations of depressive symptoms following stroke involves the selection of subjects. Many studies have included patients with prestroke histories of psychiatric illness or previous strokes (1, 11, 12). This has led to potentially confounding results, since these variables may increase the risk of depressive symptoms following stroke (12, 13). In addition, the majority of investigations have excluded many aphasic patients with impaired comprehension because of the inability of these patients to respond accurately to standardized depression scales and interviews (4, 14). Although some aspects of depressive symptoms, such as sleeping and eating disturbances, can be readily observed, internal mood state is difficult to assess in aphasic patients (15, 16). Finally, most previous studies have relied on multifactorial measures of the syndrome of depression or on psychi-

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atric diagnostic criteria (e.g., *DSM-III*) rather than on measures of specific symptoms.

The present study was undertaken to assess the relation of specific lesion locations to internal mood states and to two vegetative symptoms common in psychiatric depressive disorders, i.e., sleeping and eating disturbances. In addition to right-left and frontal-nonfrontal dimensions, lesions were classified by using a ventral-dorsal dichotomy. Patients with previous neurological or psychiatric histories were excluded, and a modification of a self-report measure of dysphoric mood was used to allow the inclusion of all but the most severely impaired aphasic patients.

METHOD

Subjects were selected from among consecutively admitted inpatients and outpatients with neurology clinic appointments at the Boston Department of Veterans Affairs Medical Center and the Braintree Hospital, a private rehabilitation facility. Before participation in the study and after explanation of the procedures, all subjects or their representatives gave informed consent. All subjects were right-handed men who had suffered a unilateral cerebrovascular accident between 1 month and 4 years before participation (mean±SD time since stroke onset was 16.2±12.3 months). Only patients whose lesions could be documented by CT scan were included. All subjects had lesions involving the cerebral hemispheres; no subjects had isolated brainstem or cerebellar lesions. Patients who had had previous cerebrovascular accidents or other disorders of the CNS were excluded, as were those with prestroke histories of psychiatric illness (including significant alcohol abuse). Aphasic patients were excluded only if their mean auditory comprehension scores on the Boston Diagnostic Aphasia Examination (17) were below the 10th percentile; only two aphasic patients were excluded by this criterion. Twenty-two aphasic patients participated. The total number of subjects was 52, and their mean±SD age was 65.8±7.9 years. Ninety percent (N=47) of the subjects were Caucasian; the remaining 10% were black. Thirty-three percent (N=17) of the subjects had high school degrees, 38% (N=20) had not completed high school, and 29% (N=15) had had some education beyond high school.

Each subject was assessed on one occasion. Self-report and interview ratings were conducted in the late morning or early afternoon to preclude effects of diurnal variation.

Instruments

Functional impairment was measured with the Modified Barthel Index of Mobility and Self Care (18) and a typical 6-point motor strength scale (19). The severity of the aphasic patients' impairment in communication was assessed by the severity score of the Boston Diagnostic Aphasia Examination.

Dysphoric mood was assessed by a modification of the Visual Analogue Mood Scale (20) in which a 100-mm line with a vertical rather than a horizontal presentation was used in order to preclude bias due to right- or left-side hemispatial neglect. The two poles were represented by words and cartoon faces indicating "happy" and "sad." The score on this Visual Analogue Dysphoria Scale was the number of millimeters from the "happy" pole. We found this modified scale to be a valid measure of dysphoric mood in a series of 95 general neurology patients referred for neuropsychological assessment, with significant correlations between scores on it and on other standardized measures of dysphoric mood, such as the MMPI depression scale and the Profile of Mood States. A similar scale has been found useful in assessing mood in stroke patients because of its brevity and its limited linguistic requirements (21). Formal assessment of reliability and validity for other vertically presented visual analogue mood scales has recently been reported (22).

The Visual Analogue Dysphoria Scale was administered as part of a larger battery of mood and depression inventories, including the Hamilton Rating Scale for Depression (23) and the Depression Adjective Checklist (24). All subjects, regardless of the severity of their aphasia, were able to provide what appeared to be reliable responses by using the Visual Analogue Dysphoria Scale. Furthermore, ratings on this scale correlated highly with scores on other standardized measures of dysphoric mood such as the Depression Adjective Checklist (r=0.81) in the aphasic patients (25), thus providing additional evidence of concurrent validity for this new mood scale. The correlation between ratings on the Visual Analogue Dysphoria Scale and the Depression Adjective Checklist existed for the aphasic subjects with the most intact auditory comprehension (r=0.84; mean±SD Boston Diagnostic Aphasia Examination auditory comprehension percentile=75.3±13.8) as well as for those with the most compromised auditory comprehension (r=0.64; auditory comprehension percentile=29.7±13.7).

Ratings of vegetative symptoms were created by using a combination of interview response and observed behavior. Sleep disturbance was assessed by a combination of the three insomnia items of the Hamilton depression scale and a 5-point rating of early morning awakening completed by a nurse familiar with the patient. Eating disturbance was similarly assessed by a combination of the two eating-related items of the Hamilton scale and a nurse's 5-point rating of diminished appetite. One patient was unable to provide meaningful responses during the Hamilton depression interview, and therefore the sleep and eating disturbance scales were composed solely of the nurse's assessments. Ratings on each of these two scales were transformed to standardized T scores (mean±SD=50±10) for the analyses.

Lesion Classification

All subjects received CT scans, which were judged independently by two members of the CT research group of the Boston Department of Veterans Affairs Medical Center Aphasia Research Center. Location of the lesions was assessed with a modification of the technique of Naeser and Hayward (26). Since all lesions were unilateral, the side of the lesion was easily determined. Analysis of intrahemispheric lesion location was performed on a region-by-region basis. Each of the following six regions was rated on a 4-point scale with respect to the percentage of infarcted tissue: the inferior frontal lobe (Brodmann's areas 10–15, 25, and 43–47), the superior frontal lobe (areas 4, 6, 8, 9, 24, 32, and 33), the temporal lobe (areas 20–22, 26–30, 34–38, and 41–43), the inferior occipital lobe (areas 17–19), the inferior parietal lobe (areas 23, 31, 39, and 40), and the superior parietal and occipital lobes (areas 1–3, 5, and 7). In order to provide intrahemispheric classifications, these ratings were then transformed using two dimensions: 1) dorsal (including the superior frontal and entire parietal and occipital lobes) versus ventral (including the inferior frontal and entire temporal lobes) and 2) frontal versus nonfrontal. A lesion was considered to be frontal if the mean rating for the two frontal regions was greater than the mean rating for the remaining four regions. Similarly, a lesion was considered to be ventral if the mean combined rating for the inferior frontal and temporal lobe regions was greater than the mean combined rating for the superior frontal, inferior parietal, inferior occipital, and superior parietal and occipital regions. The classifications, therefore, indicated whether the lesion was predominantly in one area or another, rather than solely in that area. The inclusion of inferior occipital regions in the dorsal classification was based on known corticolimbic connections rather than on actual anatomical location.

On the basis of these lesion classifications, 37% ($N=19$) of the subjects had right hemisphere lesions (63%, $N=33$, left hemisphere), 65% ($N=34$) had predominantly dorsal lesions (35%, $N=18$, ventral), and 44% ($N=23$) had predominantly frontal lesions (56%, $N=29$, nonfrontal). In this classification scheme no distinction was made between involvement of cortical and subcortical lesions.

Statistical Analyses

The relation between lesion classifications and each of the three dependent variables (i.e., ratings of dysphoria, sleep disturbance, and eating disturbance) were first assessed with a multivariate analysis of variance (MANOVA) to protect against type I error and because of intercorrelations among the dependent variables. A $2\times2\times2$ design was used, with each of the three dichotomous lesion dimensions used as a grouping variable. Individual univariate analyses of variance (ANOVAs) were performed subsequent to a significant MANOVA. The MANOVAs and ANOVAs were performed by using unweighted means analyses rather than least squares analyses, since unequal cell sizes in this sample were most likely due to chance sampling error rather than an expected inequality in the population. All analyses met the assumptions underlying univariate and multivariate analyses (e.g., homogeneity of dispersion matrices, homogeneity of variance). Significant three-way ANOVAs were followed up by appropriate simple effects tests to assess the underlying two-way interactions or main effects.

On the basis of previous research and theoretical arguments, an a priori decision was made to assess right-left by frontal-nonfrontal interactions at each of the two dorsal-ventral levels. For example, following a significant three-way interaction, two separate two-way ANOVAs were performed as simple effects tests (using appropriate error terms), one assessing the relation between side of the lesion and caudality among patients with predominantly dorsal lesions and the other assessing this relation among patients with predominantly ventral lesions. These tests, if significant, were followed up by further simple main effects tests. The relations between the dysphoria ratings and the measures of functional impairment were assessed with two-tailed Pearson correlations, as were the relations among the three dependent variables. An alpha level of 0.05 was used throughout.

RESULTS

There were no significant relations between dysphoric mood and measures of functional impairment. Specifically, rating on the Visual Analogue Dysphoria Scale was not significantly correlated with the Barthel index ($r=-0.02$, $df=50$, $p>0.05$), with the measure of motor strength ($r=0.01$, $df=50$, $p>0.05$), or with the aphasia severity score ($r=-0.19$, $df=18$, $p>0.05$).

The MANOVA assessing the relation between lesion location and depressive symptoms yielded a significant three-way interaction (Wilks' $\lambda=0.69$; approximately distributed as $F=6.16$, $df=3, 42$, $p<0.001$). There were no significant underlying two-way interactions or main effects. The subsequent univariate ANOVA with the Visual Analogue Dysphoria Scale score as the dependent variable resulted in a significant three-way interaction ($F=13.03$, $df=1, 44$, $p<0.001$). Simple effects tests resulted in two significant findings: 1) among patients with predominantly right ventral lesions, those with nonfrontal lesions had significantly greater dysphoric mood than those with frontal damage ($F=10.84$, $df=1, 44$, $p<0.01$), and 2) among patients with left dorsal lesions, those with nonfrontal lesions were more dysphoric than those with frontal lesions ($F=5.03$, $df=1, 44$, $p<0.05$) (figure 1).

The ANOVA on sleep disturbance also yielded a significant three-way interaction ($F=13.81$, $df=1, 44$, $p<0.001$). Only one follow-up simple effects test reached significance, indicating that among patients

FIGURE 1. Relation Between Lesion Location and Mean Visual Analogue Dysphoria Scale Scores of 52 Patients Following Stroke

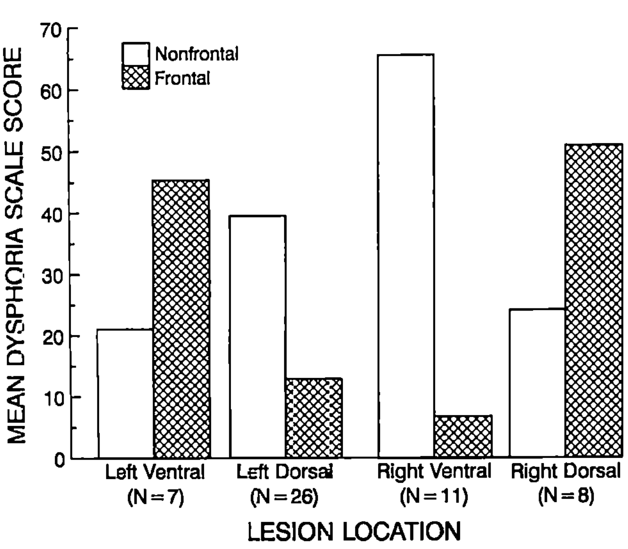
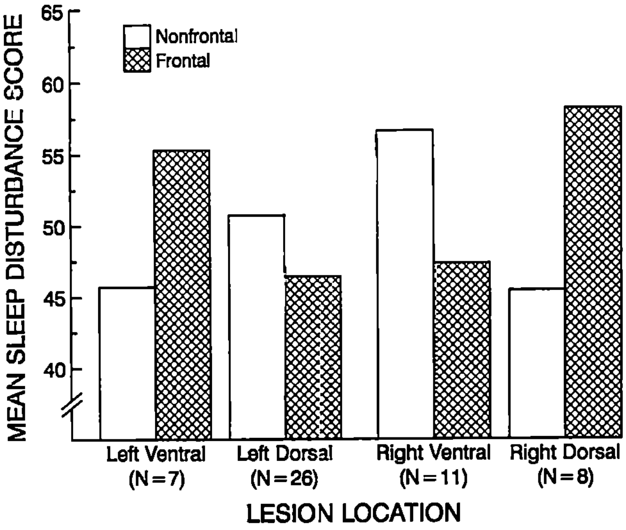


FIGURE 2. Relation Between Lesion Location and Mean Sleep Disturbance Scale Scores[a] of 52 Patients Following Stroke



[a] Standardized T scores (mean±SD=50±10).

with right dorsal lesions, those with frontal damage had greater sleeping disturbance than those with nonfrontal lesions (F=5.34, df=1, 44, $p<0.05$) (figure 2). The ANOVA on eating disturbance did not result in any significant interaction or main effect.

A comparison of mean scores on the dysphoria scale and the sleep disturbance measure among all lesion groups resulted in the following patterns. Among patients with lesions of the left hemisphere, those with predominantly parietal or occipital lesions had significantly more dysphoric mood and sleep disturbance than those whose lesions were predominantly in the superior frontal lobe. In contrast, a different pattern emerged among patients with more ventral lesions of the left hemisphere. Patients with left inferior frontal lobe lesions reported greater dysphoric mood and sleep disturbance than did those with temporal lobe lesions.

The pattern with right hemisphere lesions was quite different. Patients with right superior frontal lobe lesions reported greater dysphoria and sleep disturbance than did those whose lesions were predominantly in the right parietal or occipital lobes. Those with right temporal lesions, however, had greater dysphoria and sleep disturbance than patients with right inferior frontal lobe damage.

To assess the relations among the three different measures of depressive symptoms, we calculated Pearson correlation coefficients. There was a significant correlation between dysphoric mood and sleep disturbance, as measured by the Visual Analogue Dysphoria Scale and the sleep disturbance rating, respectively ($r=0.57$, df=50, $p<0.001$). The correlations between each of these scales and the measure of eating disturbance, however, were nonsignificant (dysphoria and eating disturbance, $r=0.19$, df=50, $p>0.05$; sleep disturbance and eating disturbance, $r=0.12$, df=50, $p>0.05$).

DISCUSSION

These results suggest that dysphoric mood following stroke is not merely an expected grief reaction to functional impairment, a finding consistent with most previous studies (3, 4). Furthermore, our findings indicate that there is a complex relationship between the location of the lesion and depressive symptoms. The three-way interactions involving right-left, dorsal-ventral, and frontal-nonfrontal lesion dimensions suggest that relying on any one of the underlying two-way interactions (e.g., side of lesion by proximity to the frontal pole) or main effects (e.g., right-left), as previous studies have done (4, 27–31), may inadequately characterize the profile of lesion location factors influencing poststroke mood disorders.

Eating disturbance was not significantly correlated with either disturbed sleeping or dysphoria in this sample of stroke patients. Furthermore, eating disturbance was not associated with lesion location. These findings suggest that following stroke, there is a dissociation between two vegetative symptoms which typically co-occur in psychiatric patients with mood disorders. It is possible that due to hospitalization, impairment in swallowing, or other variables associated with stroke, actual lesion-based differences in eating disturbance were masked. On the other hand, it is impressive that sleep disturbance correlated so well with dysphoric mood state despite the opportunity for so many non-affectively based factors to influence sleep in medically incapacitated patients (32). In addition, similar patterns of lesion foci were associated with both dysphoric mood and insomnia, suggesting a common underlying mechanism.

These findings suggest that sleep dysfunction and dysphoria may constitute part of a legitimate clinical syndrome in poststroke patients. It is still uncertain, however, whether this putative syndrome resulting from a structural brain lesion is identical to the syndrome of major depressive disorder observed in primary psychiatric patients. It should be noted that a "mood syndrome" is typically considered to be a cluster of mood and related symptoms that co-occur for a period of time (*DSM-III-R*). We focused on only two of the nonmood symptoms associated with major depressive syndrome or dysthymia (i.e., appetite and sleep disturbance). We chose these two symptoms because they are readily observed by family members and/or nursing staff and do not necessarily depend on accurate patient report. The *DSM-III-R* criteria for major depressive syndrome include several symptoms that are either difficult to assess because of aphasia, dysprosody, and other cognitive impairments (e.g., feelings of worthlessness, suicidal ideation) or may be masked or mimicked by the known neurobehavioral consequences of the stroke itself (e.g., poor concentration, apathy, psychomotor agitation or retardation). Because of these difficulties, it has been suggested that vegetative signs may be the only manifestations of poststroke mood disorders that are easily assessed (15) and that new diagnostic criteria should be developed specifically for poststroke mood disorders (33).

Robinson (34) argued that poststroke mood disorders result from disruption of ascending catecholamine pathways before they pass posteriorly around the left anterior frontal lobe. This hypothesis does not, however, adequately explain the finding that there is a dissociation between ventral and dorsal lesions within the frontal lobe (in either hemisphere) with regard to depressive symptoms following stroke. Recent evidence suggests that rather than resulting from dysfunction within a single neurotransmitter system, psychiatric depressive disorders may result from a complex interaction of neurochemical and neuroendocrine system dysfunction (35, 36). Nonetheless, our data confirm the hypothesis that lesion location is a valid and significant factor in the mix of influences which may result in a dysphoric mood state following stroke.

The method we used to assess lesion location remains relatively crude when compared to advances in other fields of neuropsychological lesion correlation (37). Greater numbers of carefully characterized stroke patients grouped according to important parameters such as lesion size and time since stroke must be collected before more sophisticated studies of lesion location can be undertaken. However, even with the limited methods available, our findings confirm the hypothesis that the dorsal-ventral lesion dichotomy represents an important and ecologically valid parameter of lesion location. If, as we suspect, the critical aspect of lesion location is the impact of the lesion on local cortical/subcortical limbic system circuitry, then the local pattern of limbic system connections should determine the effect of any given lesion. Previous reports have indicated a distinctive pattern of limbic system connections for dorsal cortical centers versus ventral cortical centers (8–10). The findings in this study provide further empirical evidence for this dorsal-ventral distinction.

It is likely that the ultimate etiology of poststroke mood disorders will reflect a complex interaction of neurochemical, neuroendocrine, metabolic, and cognitive alterations following stroke, as well as differences in both inter- and intrahemispheric cerebral specialization of emotional processing (8, 38–40). Future research that uses reliable and valid measures of specific features of the depressive syndrome, along with even more precise neuroanatomical localization, should help to further clarify these issues.

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The Nature and Course of Olfactory Deficits in Alzheimer's Disease

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Objective: The aim of this study was to determine the specific nature and course of olfactory deficits in Alzheimer's disease. Previous studies had noted impaired odor identification, but there was no unanimity about the presence of odor detection deficits. Method: Odor identification was tested in 55 patients with Alzheimer's disease and 57 elderly control subjects by using the University of Pennsylvania Smell Identification Test. Odor detection was assessed in 46 subjects with Alzheimer's disease and 40 control subjects by using a forced-choice threshold test with geraniol as the odorant. Results: Significant deficits in olfactory identification were present in subjects who were in the earliest stages of cognitive impairment, and these deficits increased as Alzheimer's disease progressed. There was some overlap in individual smell identification test scores between cognitively impaired patients and normal elderly subjects. On the other hand, odor detection deficits did not appear until Alzheimer's disease was relatively advanced. Smell identification test scores were correlated with Mini-Mental State scores, but geraniol detection was not. Conclusions: Odor identification is impaired early in Alzheimer's disease and may be more influenced by cognitive status than is acuity of odor detection, which is not altered until later in the disorder. The pattern of hyposmia in Alzheimer's disease suggests that the disorder may not "begin in the nose," as has been theorized previously. Further refinement of olfactory testing may be useful in the diagnostic evaluation of early dementia.

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There are anatomical (1, 2) and neurochemical (3–6) links between Alzheimer's disease and the sense of smell. Studies of olfactory performance in Alzheimer's disease are grounded in these observations. Early reports that noted impaired odor identification by Alzheimer's disease patients (7–9) were followed by a number of confirmatory studies (10–13).

A few groups have also tested odor detection capabilities in Alzheimer's disease. The process of odor detection is less dependent on cognition than is odor identification (14). There is also evidence that odor identification involves medial temporal lobe structures and that detection is a more peripherally based phenomenon (15). Studies have yielded conflicting data regarding the presence (10, 11) or absence (12, 13) of impaired odor detection in Alzheimer's disease.

We attempted to clarify the nature of the olfactory disturbance in Alzheimer's disease and to use it as a means of exploring other questions about this disorder.

METHOD

We administered one or more olfactory tests to 281 subjects of various ages and in different diagnostic categories, including 60 elderly control subjects between the ages of 60 and 79 and 62 patients with Alzheimer's disease. Subjects were patients, families, and staff members recruited from the New York Veterans Administration (VA) Medical Center, the Aging and Dementia Research Program of New York University, and various senior citizen centers. The screening procedure included administration of the 30-point Mini-Mental State examination (16) and the 17-item Hamilton Rating Scale for Depression. Control subjects were free of cognitive and affective complaints and scored above 27 on the Mini-Mental State and below 16 on the Hamilton scale. The diagnosis of Alzheimer's disease was established according to the criteria

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of McKhann et al. (17). Alzheimer's disease patients were also tested with the Mini-Mental State and the Hamilton depression scale and were rated on the Global Deterioration Scale, a seven-stage system designed to reflect the characteristic presentation and course of age-associated cognitive impairment and Alzheimer's disease (18). Stage 3 on the Global Deterioration Scale describes a group of patients who have early cognitive and behavioral changes but may not decline further into Alzheimer's disease (stages 4 through 7).

All subjects were screened for cognitive, medical, and psychiatric disorders that might interfere with olfactory scores (19) and thus preclude their participation. These disorders included head trauma, hypothyroidism, insulin-dependent diabetes mellitus, Cushing's disease, active hepatitis, cirrhosis, chronic renal failure, multiple sclerosis, vitamin B_{12} deficiency, and local respiratory tract factors such as active rhinitis or sinusitis (allergic or infectious), active asthma, and history of nasal polyps or surgery. Potential subjects were also not included if they were currently taking antidepressants, neuroleptics, antihistamines, or anticholinergics. Current smokers were excluded from participation. Informed consent was obtained from subjects or next of kin (if subjects were incompetent) after procedures, risks, and benefits had been explained.

The University of Pennsylvania Smell Identification Test (20) was administered to 55 Alzheimer's disease patients and 57 age-matched control subjects (60–79 years old). The test is a standardized scratch-and-sniff task involving 40 common odorants, each of which must be identified from four written choices.

To test odor detection we used a simple method designed to eliminate cognitive factors as much as possible. Three sniff bottles were presented in each of nine trials: two bottles contained odorless fluid, and a third bottle in each set contained diluted geraniol, an olfactory stimulant used in the perfume industry. The concentration of geraniol increased in each successive triad of bottles to minimize adaptation effects. The position of the geraniol bottle in each set was randomized. The threshold value was designated as the lowest of three consecutive concentrations that were correctly identified. The threshold score was designated from 1 (lowest concentration) through 9 (highest); a score of 10 signified no perception of odorant. The specific concentrations were 6.3, 9.97, 15.8, 25.0, 39.6, 62.8, 99.6, 157.9, and 250.0 cc of geraniol dissolved in enough odorless diethyl phthalate to produce one liter of fluid. Forty-six Alzheimer's disease patients and 40 age-matched control subjects were tested with this paradigm.

The study was approved by the New York VA Medical Center and the institutional review board at New York University Medical Center.

RESULTS

We compared the performance on the smell identification test of the 55 Alzheimer's disease patients and the 57 age-matched control subjects (mean±SD age=70.1±5.3 years). A one-way analysis of variance (ANOVA) demonstrated a significant difference between groups ($F=30.71$, $df=4, 111$, $p<0.004$). We found significant differences ($p<0.05$), as measured by the Scheffé post hoc test, between the control group and patients grouped according to Global Deterioration Scale stages. The mean±SD score on the smell identification test for the control subjects was 31.80±7.2. The patient groups' scores were as follows: stage 3 (N=8; mean age=69.5±13.3), 20.25±7.1; stage 4 (N=23; mean age=68.1±7.8), 20.39±10.3; stage 5 (N=14; mean age=68.3±6.2), 12.93±3.4; stage 6 (N=10; mean age=71.4±9.1), 12.50±4.7.

There were no significant differences between scores of patients at the various stages of the Global Deterioration Scale. When the stage 3 and stage 4 groups' scores were combined (20.36±9.5), their performance was significantly better ($p<0.05$) than that of the combined stage 5 and stage 6 groups (12.75±3.9).

As mentioned previously, a number of studies have found differences in smell identification between Alzheimer's disease patients and elderly control subjects. We decided to evaluate the potential utility of the University of Pennsylvania Smell Identification Test in discriminating between this type of dementia and normal aging. We chose a cutoff score of 27 to reflect a presumptive diagnosis of Alzheimer's disease for the stage 3 and stage 4 patients and a cutoff score of 23 for the stage 5 and stage 6 patients. We found that 10 (32.3%) of the 31 stage 3 and stage 4 patients scored above 27, a level of performance matched by 46 (80.7%) of the 57 control subjects ($\chi^2=20.36$, $df=1$, $p<0.05$). None of the 24 stage 5 and stage 6 subjects scored above 23 on the smell identification test, but 50 (87.7%) of the 57 control subjects did ($\chi^2=32.33$, $df=1$, $p<0.05$).

Scores on the geraniol threshold task for the combined stage 3 and stage 4 groups (N=28; mean age=68.6±9.5) and the combined stage 5 and stage 6 groups (N=18; mean age=68.6±5.6) were compared with those of the control subjects (N=40; mean age=70.2±4.9). A one-way ANOVA demonstrated a significant difference between groups ($F=5.84$, $df=2, 85$, $p<0.004$). A Scheffé post hoc analysis was performed. The stage 3 and stage 4 patients had a score of 4.46±3.4, not significantly different from that of the normal subjects (4.00±2.7). The more advanced Alzheimer's disease patients demonstrated impaired odor detection, with a threshold score of 6.94±3.4. This sample of advanced dementia patients showed worse performance than the control subjects (Scheffé $F=5.64$, $df=2, 85$, $p<0.05$) and the stage 3 and stage 4 group (Scheffé $F=3.53$, $df=2, 85$, $p<0.05$).

For the Alzheimer's disease patients there was a strong relation between performance on the smell identification test and Mini-Mental State score (Pearson's $r=0.48$, $df=54$, $p<0.005$) but not between odor threshold score and Mini-Mental State score ($r=-0.13$, $df=45$, n.s.).

DISCUSSION

These results suggest several points about the course of the olfactory changes in Alzheimer's disease. Particular attention should be paid to the data on subjects at stage 3 of the Global Deterioration Scale because of the uncertainty of the diagnosis of dementia. Not all stage 3 patients decline further into Alzheimer's disease; in fact, in one study only 25% of 36 stage 3 subjects had reached stage 4 after 3.5 years (Barry Reisberg, personal communication, 1989). Some of these stage 3 patients may have had hyposmia, which might predict decline. As we have noted, our stage 3 group showed impaired performance on the smell identification test; their scores were not different from those of the stage 4 patients. It is possible that most of the stage 3 patients will ultimately become demented and that the hyposmia is an early indicator. It appears that loss of olfactory acuity should be evaluated further as an early marker for Alzheimer's disease.

There are deficits in both odor detection and odor identification in Alzheimer's disease. The loss of ability to identify odors begins early, perhaps as a harbinger of disease, and is progressive. The change in detection acuity is a later phenomenon that appears in advanced stages of the disease. This pattern of hyposmia explains the contradictory findings in earlier studies. The two studies that found no impaired detection recruited patients with "mild" Alzheimer's disease (12, 13). On the other hand, higher thresholds were present in a group of subjects with predominantly moderate Alzheimer's disease (11) and in a sample that contained patients who had "rather advanced dementia" (10).

The finding that for patients with Alzheimer's disease there is a significant correlation of Mini-Mental State scores with odor identification performance but not with odor thresholds suggests several conclusions. Odor identification is impaired early and seems to be more influenced by cognitive status than is acuity of odor detection. Although thresholds do change from stages 3 and 4 to stages 5 and 6, it appears that the change may be less uniform than it is for smell identification and is limited to the higher levels of cognitive deficit.

The differences in time course for changes in odor detection and identification in Alzheimer's disease may call into question the theory that more peripheral structures are the earliest to be involved. Roberts (21) hypothesized a process whereby aluminosilicates enter the nasal mucosa and, through retrograde absorption into the CNS, lead to a cascade of events culminating in Alzheimer's disease. One might expect odor detection to be impaired early in the disease and odor identification later if this is true, but the pattern of olfactory deficit that we found is the reverse of this hypothetical picture. It could be that the physiological processes involved in odor detection are more redundant and resistent to functional change than those which are involved in identification, but so far there is no evidence for this.

The utility of olfactory testing for differential diagnosis of dementia is limited at this time. An overlap of scores with those of patients with other disorders (e.g., multi-infarct dementia; Serby et al., unpublished data) and with scores of normal elderly subjects restricts the feasibility of this approach. This is especially true because the greatest overlap occurs in the earliest phases of Alzheimer's disease, when diagnosis may be obscure. The greatest potential for such clinical tests rests in the possibility that olfactory dysfunction is an early marker of pathological changes in otherwise "normal" geriatric subjects. It is clear that hyposmia is an inherent part of the Alzheimer's disease process. However, refinement of olfactory testing is an essential prelude to development of a diagnostic tool. Olfactory testing may prove to be more useful in combination with other diagnostic procedures.

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Nonfearful Panic Disorder in Neurology Patients Validated by Lactate Challenge

Johnna L. Russell, M.D., Matt G. Kushner, M.A.,
Bernard D. Beitman, M.D., and Kim M. Bartels, B.S.

Objective: Nonfearful panic disorder meets the DSM-III-R *criteria for panic disorder but is not associated with subjective fear and anxiety. The authors determined its prevalence in a group of neurology patients and assessed its diagnostic validity as a panic disorder subtype by evaluating the response of the patients with nonfearful panic disorder to sodium lactate and antipanic pharmacotherapy. Method: The subjects were all neurology patients referred over 1 year to a university hospital's psychiatric consultation service because of negative medical workups for their symptoms (N=48). Patients who met the* DSM-III-R *criteria for panic disorder but did not report subjective anxiety or fear during panic episodes were diagnosed as having nonfearful panic disorder. Afterward, each of those patients received a sodium lactate infusion and, 5 hours later, a sodium chloride infusion. They were then treated with antipanic medication and followed for at least 6 months. Results: Of the 48 neurology patients referred for psychiatric evaluation, 11 (23%) met the criteria for panic disorder, and all 11 met the criteria for nonfearful panic disorder. All 11 responded positively to lactate but not to placebo, and they each experienced an at least 75% reduction in symptoms during the 6-month follow-up period. Detailed case reports of three of these patients are presented. Conclusions: These findings support the construct and predictive diagnostic validity of nonfearful panic disorder as a subtype of panic disorder and suggest that a lack of attention to this group leads to both the underestimation of the prevalence of panic disorder and to the withholding of potentially successful treatments for this group.*

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Many early descriptions of panic anxiety did not include reports of subjective fear. Freud (1) noted that panic anxiety could become associated with a disturbance of one or more of the bodily functions such that the patient "complains of 'spasms of the heart,' 'difficulty breathing,' and such like; in his description, the feeling of anxiety often recedes into the background" (p. 86). Similarly, panic-like syndromes (e.g., "Da Costa's syndrome," "neurocirculatory asthenia," "irritable heart syndrome," and "effort syndrome") were described by early physicians in terms of somatic symptoms without reference to subjective fear (2).

Although early descriptions did not focus on subjective fear as an essential element of the panic anxiety syndrome, *DSM-III* established fear as a central feature of the panic disorder diagnosis. According to *DSM-III-R,* however, individuals who experience panic attacks without self-reported fear can technically be given the diagnosis of panic disorder. Specifically, whereas *DSM-III* required a report of episodes involving intense "fear" or "apprehension" before questioning concerning panic disorder should continue, *DSM-III-R* requires reports of episodes of intense "fear" or "discomfort." This change broadened the range of individuals to whom the diagnosis of panic disorder applies to include those who do not report subjective anxiety accompanying their attacks ("nonfearful panic disorder").

The existence of individuals who experience panic-attack-like episodes that do not include self-reported fear or anxiety is now well documented (the relevant literature was reviewed by M.G. Kushner et al. in their report to the *DSM-IV* anxiety task force in 1990). For example, in two groups of cardiology patients, Beitman et al. (3, 4) found that 31.6% and 40.0%, respectively, of those meeting the *DSM-III-R* criteria for panic disorder reported attacks that included discom-

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fort and somatic symptoms in the absence of subjective fear. Katon et al. (5) found that in addition to the 13.3% of their primary care patients who met the *DSM-III* criteria for the diagnosis of panic disorder (which excludes nonfearful panic disorder), another 2.6% of the patients met the full *DSM-III* panic criteria except that their attacks involved somatic panic symptoms in the absence of self-reported fear (i.e., nonfearful panic disorder). Rachman et al. (6) found that approximately 33% of their 20 panic disorder patients reported panic attacks in the absence of any fear-related cognitions ("non-cognitive panic").

Although nonfearful panic disorder has been systematically assessed in medical patients only in cardiology and primary care settings, several case reports (7, 8) have documented panic attacks without fear in neurology and gastroenterology patients, who were described as experiencing "alexithymic panic disorder" or "masked anxiety." Thus, one purpose of our study was to systematically determine the prevalence of nonfearful panic disorder in a group of neurology patients.

Beyond documenting the presence of nonfearful panic disorder in various populations, it is important to address the nosological validity of nonfearful panic disorder as a subdiagnosis of panic disorder. Even though *DSM-III-R* technically allows for the inclusion of patients with nonfearful panic disorder under the heading of panic disorder, to our knowledge virtually no empirical evidence concerning the diagnostic validity of nonfearful panic disorder as an anxiety disorder has been reported in the literature (M.G. Kushner et al.). To confirm predictive validity, for instance, it is necessary to demonstrate that the response of patients with nonfearful panic disorder to antipanic medications is similar to the response of other panic patients. Also, tests of the construct validity of nonfearful panic disorder as an anxiety disorder have not been conducted with patients who have nonfearful panic disorder. For example, because sensitivity to lactate is thought to be a marker for panic disorder (9), determining whether patients with nonfearful panic disorder are also lactate sensitive may be one way of determining the construct validity of this diagnosis. Thus, a second purpose of this study was to assess the response of patients with nonfearful panic disorder to both sodium lactate challenge and antipanic pharmacotherapy.

METHOD

Over 1 year we screened all neurology patients referred to a university hospital's psychiatric consultation service for evaluation because of negative medical workups for their symptoms; all 48 patients gave informed consent for this study. On the basis of a diagnostic interview following the format of the Structured Clinical Interview for DSM-III (SCID) (10), one of us (J.L.R.) classified patients as having nonfearful panic disorder if they met the *DSM-III-R* criteria for panic disorder but did not report having subjective anxiety or fear during panic episodes (i.e., they denied episodes that involved fear in any way and specifically denied fear of dying, fear of going crazy, and fear of losing control).

After the diagnostic interview, one of us (J.L.R.) challenged the patients who met the criteria for nonfearful panic disorder with a 0.5-M sodium lactate infusion and a 5% dextrose with 0.5-N sodium chloride (placebo) infusion. The lactate and placebo were infused approximately 5 hours apart, and a research assistant ensured that the order of administration was random and unknown to both the administrator and the patient (i.e., double-blind). The patients were said to have responded positively to the lactate if they later reported that during the lactate infusion (but not the placebo infusion) they had experienced either 1) a recurrence of the symptoms that originally led them to seek treatment or 2) a classic panic attack that involved fear. (We used a clinical measure because of the patients' difficulty in communicating during lactate infusion.) Patients whose symptoms persisted longer than 5 minutes after discontinuation of the lactate infusion were administered 1 mg of lorazepam intravenously. Finally, all patients with nonfearful panic disorder were treated with an antipanic medication after the lactate procedure and were then followed over a minimum of 6 months.

RESULTS

Of the 48 neurology patients who were referred for psychiatric evaluation, 11 (23%) met the criteria for panic disorder, and all of these 11 met the criteria for nonfearful panic disorder. Four of these 11 complained primarily of "dizzy" spells, three complained of "pseudoseizures" (or falls with movement), two complained of syncope (with claimed loss of consciousness), one complained of "vertigo" spells, and one complained of parasthesias.

All 11 patients with nonfearful panic disorder responded positively to lactate but not to the placebo infusion. The responses to lactate of eight patients included the same cluster of symptoms that led them to seek neurological evaluation (i.e., they did not report fear), although three patients responded with classic panic attacks (i.e., they did report fear). The patients who experienced fear indicated that this aspect of the attack was significantly different from their usual episodes. All 11 patients with nonfearful panic disorder required lorazepam, 1 mg i.v., to terminate their induced episodes.

In addition to responding positively to lactate infusion, all 11 of the patients with nonfearful panic disorder responded positively to treatment with antipanic medication (clonazepam or imipramine), i.e., they experienced an at least 75% reduction in symptoms over the 6-month follow-up period.

CASE REPORTS

Case 1. Mr. A, a 57-year-old white factory worker, was referred by his neurologist after he had been seen many times in the emergency room and by his internist for complaints of "vertigo." He had a 6-month history of recurrent dizzy spells; he said that during these spells the room seemed to spin around him. Mr. A was evaluated extensively by the neurology department and the ear, nose, and throat department. The examinations included electronystagmogram, MRI, somatosensory and auditory evoked potentials, heavy metal screen, lumbar puncture, thyroid function tests, and folate and B_{12} measurements. No cause for the disturbance was found. A 24-hour EEG and Holter monitor ECG showed no evidence of seizure episodes or cardiac dysrhythmia, in spite of Mr. A's report of a dizzy spell during monitoring. He was referred to the psychiatry department because a diagnosis of "conversion disorder" was considered. When seen in consultation, Mr. A did not appear depressed, but he described increasing constriction of his life to avoid these attacks, which he said occurred primarily when he was going to work, to shopping malls, or to the grocery store. In addition to the dizziness, he reported that during the attacks his heart pounded and he sometimes felt as though he were floating out of his body, but he specifically denied any feelings of anxiety or nervousness. Mr. A had been given a trial of meclizine and various phenothiazines, but they had not relieved his symptoms at all. A sodium lactate infusion was carried out in the double-blind fashion described earlier. During the lactate infusion Mr. A experienced a recurrence of his "dizzy spells," which were accompanied by rotatory sensations and other autonomic panic symptoms. These symptoms were alleviated almost immediately by injection of 1 mg of lorazepam. Mr. A was placed on a regimen of imipramine, 50 mg h.s., and the dose was increased over 6 weeks to 250 mg/day. He experienced marked symptomatic relief and was free of symptoms at the 6-month follow-up.

Case 2. Ms. B, a 34-year-old teacher, developed periodic severe parasthesias in her hands and legs in a stocking-glove distribution. The parasthesias in her legs tended, over 10–15 minutes, to march in a cephalad direction and to end with a burning sensation in her pelvis. Ms. B had been seen by neurologists, gynecologists, and an internist, and no etiology for her symptoms had been discovered. A hysterectomy did not relieve the recurrent pain. She experienced some initial insomnia and intermittent anorexia, and the onset of symptoms coincided with the revelation by her husband of 17 years that he had been having an extramarital affair and desired a divorce. The workup for Ms. B included a CT scan, multiple neurologic examinations, a heavy metal screen, a glucose tolerance test, a lumbar puncture, an MRI, and measurement of B_{12}, folate, antinuclear antibodies, and evoked potentials. All results were normal. A local neurologist had prescribed thioridazine, which resulted in exacerbation of Ms. B's symptoms. (One study has found that phenothiazines can exacerbate panic attacks [11].) Ms. B was referred for psychiatric evaluation with the diagnosis of "hysteria."

Upon referral Ms. B appeared mildly depressed, although she denied feeling this way and did not meet the criteria for major depression. She communicated concerns about trying to manage her life and support two children with her salary from teaching school. Her mother had a history of "nervous asthma" spells. After the double-blind lactate infusion, Ms. B indicated that her parasthesias and other autonomic panic symptoms had been reproduced. She was given phenelzine, 15 mg b.i.d., and the dose was increased to a total of 60 mg/day, resulting in relief of her symptoms. She remained in psychotherapy and pharmacotherapy and had experienced marked remission of her symptoms at the 6-month follow-up evaluation.

Case 3. Dr. C, a 31-year-old surgeon, was referred by his neurologist because of attacks of near syncope, during which he felt as though he were going to lose consciousness, although he reported no episodes that involved actual loss of consciousness or falling. These attacks had been occurring for 6 months, chiefly when he was beginning vascular operations. Dr. C had no prior psychiatric history and stated that he did not feel he needed psychiatric consultation, although he admitted to increased stress at work after the loss of his new partner approximately 10 months earlier. He also related having lost a patient in surgery for the first time in his career approximately 8 months before the evaluation and 1 month before the onset of his recurrent episodes. His family history included depression and anxiety attacks in his "whiny, worthless mother," who had "deserted" his surgeon father when Dr. C was 10 years old. He described himself and his father as perfectionists. His father had died in surgery about 1 year before Dr. C entered medical school.

Dr. C stated that during his episodes he felt as though "lights were going to go out" and he had difficulty breathing and perspired heavily. He said that he did not experience anxiety during the episodes, although he was beginning to feel worried when entering the operating room about having another attack and had cut back on his operating schedule. Dr. C denied symptoms of major depression, although he appeared mildly depressed at the time of the interview.

Previous Holter monitoring, coronary artery study, CT scan, lumbar puncture, MRI, thyroid function tests, and B_{12} and folate measurements had yielded normal results. Double-blind lactate infusion resulted in replication of Dr. C's presenting symptoms. He was placed on a regimen of imipramine, 75 mg h.s., and experienced relief of his symptoms with a dose of 150 mg h.s. At 6-month follow-up, he was free of symptoms.

DISCUSSION

We found that 23% of neurology patients with negative medical workups who were referred for psychiatric consultation met criteria for nonfearful panic disorder. Because a diagnosis of nonfearful panic disorder is not typically considered for such patients (M.G. Kushner et al.), our results indicate that panic may be substantially underdiagnosed in such groups. The clinical importance of these findings is highlighted by the positive response of our patients with nonfearful panic disorder to standard pharmacotherapy for panic disorder.

Furthermore, our finding that patients with nonfearful panic disorder are sensitive to lactate and respond to antipanic medication provides qualified support for the predictive and construct validity of nonfearful panic disorder as a bona fide panic disorder subtype. That is, this study provides the first systematic data that associate nonfearful panic disorder with conventional panic disorder beyond the level of descriptive symptoms. Thus, we believe that increased attention to nonfearful panic disorder in the construction of future nosological systems is warranted.

Our patients denied having fearful ideation during their attacks, raising the question of what can account for these atypical symptoms? First, because we can not know what patients actually experience during panic attacks, self-report measures are inherently limited. Many people are poor witnesses of their own emotional experiences (12). Also, studies suggest that there are idiosyncratic and cultural differences in how individuals construe and report the symptoms of highly similar syndromes (13). Aside from the limitations of self-reporting, it may be important to consider patients' possible motivations for denying cognitive panic symptoms. For example, nonfearful panic disorder may involve reporting biases influenced by stoicism, shame over having "mental" (versus "physical") symptoms, and potential secondary gains associated with a "physical" but not a "mental" problem. Our clinical impression is that our patients were heterogeneous with respect to these characteristics.

In spite of the factors just mentioned, this study must be interpreted within the context of its methods. For example, although lactate was infused in a double-blind fashion, administration of antipanic medication was not blind, and thus positive responses to treatment could have been due to an uncontrolled placebo effect or a clinical bias. Perhaps of greater concern, the cases presented in this report do not rule out the possibility that neurology patients, in general, tend to be sensitive to lactate. That is, even if a positive response to lactate is a highly sensitive index of nonfearful panic disorder (a conclusion consistent with the cases we report), it is important to demonstrate that such a response is also a specific index of nonfearful panic disorder. However, studies showing that responsiveness to lactate is both sensitive and specific in panic (9) buttress our conclusion that nonfearful panic disorder is a valid panic subtype and that response to lactate is specific in this panic subtype.

The 100% response to the lactate challenge, although not contrary to study predictions, was higher than expected on the basis of previous studies (9). One possible explanation for this result is the small number of patients (N=11). For example, we studied 30 patients with chest pain who had nonfearful panic disorder and found that 87% responded to lactate (unpublished data). Therefore, a larger group might show greater variation in response to lactate infusion.

Alternatively, the higher than expected sensitivity of patients with nonfearful panic disorder to lactate might be a function of our methods. For example, if panic response had been objectively (versus clinically) defined and blindly assessed in the presence of a control group, fewer positive responses might have been found. Future studies should address these methodological concerns.

To conclude, accumulating evidence suggests that patients with nonfearful panic disorder represent a nontrivial group of difficult-to-diagnose medical patients for whom medical workups are negative. Methodological limitations notwithstanding, these findings suggest that, in addition to cardiology (3, 4) and primary care (5) patients, patients seen in neurology settings may also have noteworthy prevalences of nonfearful panic disorder. Positive responses to lactate by these patients lend substantial credence to the nosological validity of nonfearful panic disorder as a panic disorder subdiagnosis. Perhaps of greater significance, the finding that these patients respond to antipanic medications suggests that it is clinically prudent to consider nonfearful panic disorder when assessing psychiatric problems in medical populations.

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Characteristics of 60 Adult Chronic Hair Pullers

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Objective: This study was constructed to detail the demographic and phenomenological features of chronic hair pullers as well as to assess psychiatric comorbidity in a sizable study group. Method: Subjects were drawn from an outpatient population of chronic hair pullers who had been referred to a trichotillomania clinic or had responded to a newspaper advertisement announcing a treatment study of adults who pull out their hair. Sixty adult chronic hair pullers completed a semistructured interview that focused on their hair-pulling behavior and demographic characteristics and that incorporated screening questions for DSM-III-R *axis I disorders. The data were tabulated to derive a comprehensive picture of this group. Results: The typical subject was a 34-year-old woman who had pulled hair from two or more sites for 21 years. All subjects described either tension before or relief/gratification after pulling hair from the primary site, but 17% (N=10) failed to describe both of these characteristics and thus failed to fulfill the* DSM-III-R *criteria for trichotillomania. Forty-nine subjects (82%) qualified for past or current axis I diagnoses other than trichotillomania. Several characteristics of the study group suggested phenomenological differences between obsessive-compulsive disorder and trichotillomania. Conclusions: Adult trichotillomania is a chronic disorder, frequently involving multiple hair sites, and is associated with high rates of psychiatric comorbidity. Its relation to obsessive-compulsive disorder requires further clarification. The tension-reduction requirement in* DSM-III-R *for the diagnosis of trichotillomania may be overly restrictive.*

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Trichotillomania, a disorder characterized by failure to resist impulses to pull out one's hair, was first described by Hallopeau a century ago (1). Although trichotillomania is recognized as a distinct psychiatric disorder classified in *DSM-III-R* under impulse control disorders, most references to it are limited to case reports and descriptions of small series of patients. Larger studies have had sample sizes of 16 (2), 19 (3), 21 (4), 26 (5), and 34 (6). One report in the dermatological literature retrospectively characterized 145 patients, but without reference to psychiatric descriptors (7).

Trichotillomania has been described as a chronic condition (3, 6), primarily affecting females (3, 4, 7), with onset usually occurring in early childhood or adolescence (3, 7, 8). Some authors have discounted the usual chronic nature of the disorder, however, and instead characterize the condition as frequently benign and often remitting after a brief course with or without treatment (7).

A fragmented clinical picture of trichotillomania can be constructed from descriptions in the literature of patterns of hair pulling, associated behaviors, and comorbidity with other psychiatric disorders (2–4, 6–13); however, few of these variables have been studied together in a single large group of subjects. The purpose of the present study was to construct a detailed demographic and phenomenological picture of chronic hair pullers and to assess psychiatric comorbidity by using a semistructured clinical interview in a single sizable study group.

METHOD

Subjects were drawn from two sources: patients referred to the trichotillomania clinic at the University of Minnesota for evaluation and persons responding to newspaper advertisements announcing an 18-week treatment study of adults who pull out their hair. There were no statistical differences between partici-

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pants drawn from the two sources in age, gender, age at onset of hair pulling, and primary hair site involved. Subjects 18 years of age or older who completed the Minnesota Trichotillomania Assessment Inventory, a 90-minute semistructured instrument (available from the first author on request), constituted the study group. Persons under age 18 were excluded from the investigation because one source, newspaper recruitment, limited potential subjects to adults, as specified by the treatment study protocol. The trichotillomania inventory focused on the characteristics of hair-pulling behavior and the demographic characteristics of the subjects, as well as on the presence of other repetitive behaviors; it also incorporated screening questions for *DSM-III-R* axis I disorders. When screening questions suggested the presence or history of a psychiatric disorder, more detailed questioning aside from the Minnesota Trichotillomania Assessment Inventory format was pursued until a diagnosis was accepted or rejected according to *DSM-III-R* criteria. All subjects were seen between December 1988 and January 1990 and interviewed by one interviewer (G.A.C.), a senior psychiatry resident who was not blind to the subjects' histories of hair pulling.

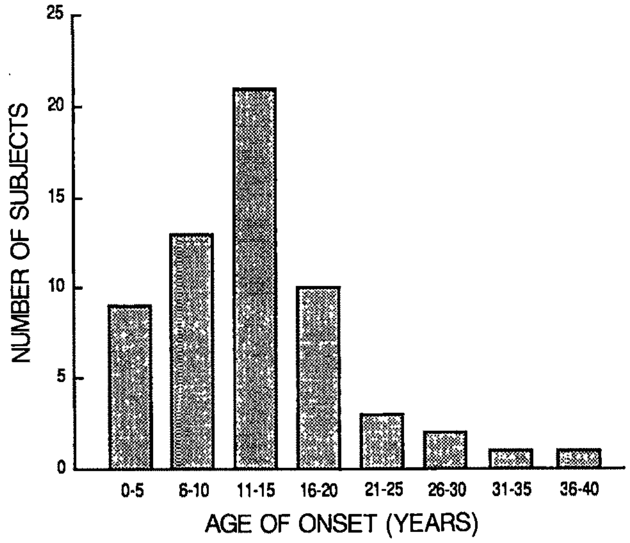
Sixty-seven potential subjects were identified. Seven did not meet the inclusion criteria: two were under 18 years of age, and five were interviewed before the development of the trichotillomania inventory. Of the remaining 60 subjects, 34 had responded to the newspaper advertisement and 26 had been referred to the trichotillomania clinic.

RESULTS

Fifty-six female and four male hair pullers were studied. The age of the subjects at the time of presentation ranged from 18 to 61 years (mean±SD=34±8, median=33). The sample included 55 white, two black, two Native American, and one Mexican-American subjects. Twenty-seven (45%) of the subjects were married, 21 (35%) were single, nine (15%) were divorced, two (3%) were separated, and one (2%) was widowed. Seven (12%) had a high school education or a General Equivalency Diploma, 19 (32%) had some college or trade school education, two (3%) had completed trade school, 26 (43%) had college degrees, and three (5%) had obtained graduate degrees.

The reported age at onset of hair pulling varied from less than 1 year (hair pulling had been present by age 1, as reported to the subject by her mother) to 39 years (figure 1); the mean±SD age at onset was 13±8 years (median=12); the mean duration of hair pulling was 21±10 years. Only three subjects (5%) had begun to pull out hair in response to a skin or scalp disease, with this behavior continuing unrelated to these conditions. Only one subject recalled a history of scalp trauma that coincided with the development of hair pulling.

FIGURE 1. Age at Onset of Hair Pulling in 60 Subjects



Twenty-three subjects pulled hair from a single site throughout the course of their illness. Of 37 subjects who pulled hair from more than one site, 32 added sites as the condition continued. Eight of these subjects began by pulling out scalp hair, 15 by pulling out eyelash hair, and six by pulling out hair from multiple sites at once. The mean±SD interval between the onset of hair pulling from one or several sites and the onset of hair pulling from an additional site or sites was 8±8 years (median=5, range=1–35). Few subjects stopped pulling hair from any site once this had become a regular pattern. Occasionally, hair pulling had occurred briefly in early childhood followed by an absence of hair pulling until the teen years, when it recurred and continued on a chronic course.

Clinical Characteristics

Forty (67%) of the subjects pulled hair primarily from the scalp; 13 (22%) pulled primarily eyelashes, five (8%) primarily eyebrows, one (2%) primarily facial hair, and one (2%) primarily pubic hair.

Twenty-three (38%) pulled hair from one site only. Thirty-seven (62%) pulled hair from two or more, 20 (33%) from three or more, and six (10%) from four or more. Table 1 details the number of subjects who reported pulling hair from specific sites at some time during the course of their disorder. Forty (89%) of the 45 scalp hair pullers reported pulling some hair from the vertex of the scalp, 31 (69%) from the temporoparietal scalp, 26 (58%) from the occipital scalp, and 27 (60%) from the frontal scalp. Although they were not routinely asked, five (8%) of the 60 subjects reported having pulled hair from a child's scalp or eyelashes, and two (3%) had pulled hair at some time from a spouse or significant other.

Severity of hair loss varied from minimal but visible hair thinning to nearly total depilation of involved sites. The majority of subjects disguised their loss well, usually by styling their hair or by applying makeup to

TABLE 1. Sites From Which 60 Subjects Pulled Hair

Site	N	%
Scalp	45	75
Eyelashes	32	53
Eyebrows	25	42
Pubic area	10	17
Beard/face	6	10
Mustache	4	7
Arm	6	10
Leg	4	7
Chest	2	3
Abdomen	1	2

eyelashes or eyebrows so that the hair loss would not be noticeable to the casual observer. Several scalp hair pullers required wigs.

Thirty-six (60%) of the subjects reported an asymmetrical pattern of hair pulling with predominant right- or left-side hair loss, whereas 24 (40%) pulled out hair in a symmetrical pattern. Fifty-two (87%) of the subjects were right-handed, and eight (13%) were left-handed. Twenty-six subjects reported the hand with which they pulled their hair out; 10 (38%) of these subjects pulled with the dominant hand, 10 (38%) pulled with the nondominant hand, and six (23%) pulled equally with both hands.

Subjects who primarily pulled out scalp hair reported a mean±SD of 27±30 (median=16) episodes of hair pulling per week. Those who primarily pulled out eyelash hair reported 15±17 (median=7) episodes per week (one subject reported 385 episodes per week and was excluded from determination of mean and median).

Forty-one (68%) of the subjects pulled out single hairs only, whereas three (5%) reported pulling out only groups or tufts of hair. Sixteen (27%) pulled out a combination of single hairs and groups of hair. Sixteen subjects (27%) pulled out only short or early-growth hair, seven (12%) pulled out only full-length hair, and 37 (62%) pulled out a combination. Thirty-four (57%) of the subjects volunteered that hairs perceived as coarse or thick were more likely to be pulled out than hairs without such qualities.

All subjects used their fingers to pull out hair, and 26 (43%) also reported having used tweezers at some time to remove hair for other than cosmetic reasons. One patient rubbed hair off in addition to pulling it out, and another frequently used scissors to cut hair short in addition to the hair pulling.

Eight subjects (13%) reported pruritus in the area of hair pulling but denied that the pruritus was related to the hair pulling; five (8%) of the subjects reported that hair pulling was usually initiated in response to pruritus. One additional subject reported a history of pruritus leading to hair pulling, which had since resolved. Six subjects (10%) reported that pruritus occurred as a result of hair pulling.

Seventeen (28%) of the subjects usually experienced pain when pulling out hair. An additional two (3%) described pain only in association with pulling from certain sites (i.e., eyelashes, beard). Forty-one (68%) of the subjects denied that hair pulling was painful, although for two of these, hair pulling had been painful in the past.

Twenty-nine (48%) of the subjects reported at least one of several oral behaviors associated with hair pulling. Fifteen (25%) rubbed hair around their mouths after pulling it out, whereas five (8%) licked and six (10%) ate their hair. Twenty (33%) chewed or bit off the ends of hair. No subjects reported a history of abdominal symptoms or trichobezoars as a result of hair ingestion, although one reported noticing hair in her stool.

Fifty-seven (95%) of the subjects reported an increasing sense of tension before pulling out their hair (criterion B for *DSM-III-R* trichotillomania), and 53 (88%) reported gratification or a sense of relief after pulling out their hair (criterion C for *DSM-III-R* trichotillomania); all subjects acknowledged at least one of these two characteristics. Ten subjects (17%), therefore, did not satisfy the *DSM-III-R* criteria for a diagnosis of trichotillomania. Interestingly, of the 37 subjects who pulled hair from multiple sites, 13 (35%) experienced mounting tension only when pulling hair from certain sites. Similarly, 16 (43%) experienced gratification after pulling hair from only some sites; for example, those who primarily pulled out scalp hair often described mounting tension and relief associated with doing this but frequently denied having these feelings when pulling out eyelash, eyebrow, or pubic hair. Several subjects described increased gratification associated with removal of specific hair types such as gray hair, coarse hair, or hair with intact roots. All subjects viewed their hair pulling as excessive or unusual behavior.

Nine (15%) of the subjects said that their focus of attention was primarily on hair pulling when it occurred. Three (5%) reported that hair pulling always occurred without their full awareness, and 48 (80%) reported a combination varying between full and incomplete awareness. Twenty-six subjects (43%) described episodes of hair pulling that would start with incomplete awareness and then develop into full awareness, although this pattern was routinely inquired about only after we had had some initial experience with this kind of report.

Fifty-nine (98%) of the 60 subjects actively attempted to resist hair pulling, often applying a wide range of techniques (table 2). Fifty-two (87%) of the subjects attempted to disguise hair loss. Of the 45 who pulled out scalp hair, 13 (29%) had worn wigs, 16 (36%) had worn scarves or hats, and 23 (51%) had styled their hair in attempts to hide bald spots or hair thinning. Of the 32 subjects who pulled out eyelashes, 11 (34%) had tried wearing false eyelashes. Four (11%) of the 35 subjects who pulled out eyelash and/or eyebrow hair wore eyeglasses to hide hair loss, and 24 (69%) had used makeup for this purpose.

Hair pulling frequently occurred while subjects were engaged in sedentary activities. Forty-three (72%) of

TABLE 2. Methods Used by 60 Subjects in Attempts to Resist Hair Pulling

Method	N	%
Barrier on head	20	33
Change in activities	13	22
Keeping hands occupied	12	20
Wearing mittens/gloves	12	20
Sitting on hands	9	15
Taping fingers together	5	8
Altering fingernails	5	8
Hiding tweezers	4	7
Chewing gum	3	5
Petroleum jelly on hands/hair	3	5

TABLE 3. Lifetime Prevalence of Psychiatric Disorders in 60 Subjects Who Were Chronic Hair Pullers

Diagnosis	N	%
Trichotillomania	50	83
Mood disorders		
Major depression	33	55
Dysthymia	5	8
Bipolar disorder	0	0
Bipolar disorder not otherwise specified	2	3
Psychotic disorders		
Schizophrenia	0	0
Schizoaffective disorder	1	2
Anxiety disorders		
Panic disorder without agoraphobia	4	7
Panic disorder with agoraphobia	7	12
Agoraphobia	2	3
Obsessive-compulsive disorder	9	15
Generalized anxiety disorder	16	27
Social phobia	5	8
Simple phobia	19	32
Eating disorders		
Bulimia nervosa	5	8
Anorexia nervosa	0	0
Eating disorder not otherwise specified	7	12
Substance abuse/dependence		
Alcohol	11	18
Other	10	17
Other		
History of separation anxiety disorder	4	7
Tourette's disorder	0	0

the subjects pulled hair while watching television, 40 (67%) while reading, 30 (50%) while talking on the telephone, 24 (40%) while lying in bed, 22 (37%) while driving, and 15 (25%) while writing or doing paperwork. Thirty-two (53%) of the subjects pulled out hair only when they were alone, 15 (25%) pulled out hair only when they were alone or with their immediate families, and 13 (22%) pulled out hair in the presence of persons other than family members; however, all subjects pulled out hair primarily while they were alone.

Fifty-six subjects reported diurnal variation in hair pulling, worse in the evening for 53 (95%) and worse in the morning for three (5%). Eleven (20%) of the 56 female subjects reported increased hair pulling premenstrually; one subject pulled out hair only in the premenstrual period.

Two subjects (3%) described histories of self-inflicted burns, and three subjects (5%) had histories of self-cutting. No subjects had engaged in self-choking. Two subjects (3%) had histories of repetitively hitting themselves, and one of these had produced other injuries (placed her hand in a blender, dropped a storage trunk lid on her hand) to gain attention from her parents.

Subjects were routinely asked whether nail biting, knuckle cracking, nose picking, thumb sucking, tongue chewing, cheek chewing, lip biting, head banging, body rocking, scab picking, and picking at acne were frequent problematic behaviors either currently or in the past. Fifty-one (85%) of the subjects reported histories of one of these behaviors. The prevalence of these specific habits compared to the prevalence in a control group will be reported in a separate paper.

Comorbidity

Table 3 summarizes comorbidity results for the *DSM-III-R* axis I disorders that were routinely screened for. Only 11 (18%) of the subjects did not receive diagnoses of current or past axis I disorders other than trichotillomania.

The lifetime prevalence of mood disorders (including one case of schizoaffective disorder) was 65%. Fourteen (23%) of the subjects met the criteria for current major depression and nineteen (32%) for a history of major depression. Two of these subjects gave histories of major depression superimposed on dysthymia. An additional three subjects were given diagnoses of dysthymia alone. Two subjects received diagnoses of bipolar II disorder (bipolar disorder not otherwise specified).

A lifetime prevalence of 57% for anxiety disorders was noted. Eleven subjects (18%) reported current and/or past panic disorder or panic disorder with agoraphobia. Six (10%) of the subjects met the criteria for current obsessive-compulsive disorder, and three (5%) had histories of the disorder. Eleven (18%) of the subjects reported present and/or past obsessions or compulsions that were both frequent and ego-dystonic, but they did not meet the criteria for the disorder.

Twelve (20%) of the subjects had current or past eating disorders. Substance use disorders were present in 13 (22%) of the subjects: abuse of alcohol in 18% (N=11), of amphetamines in 5% (N=3), of cannabis in 5% (N=3), of cocaine in 3% (N=2), and of hallucinogens in 3% (N=2).

DISCUSSION AND CONCLUSIONS

This study examined the characteristics of a large group of adults with chronic hair pulling. The results showed that chronic hair pulling most often begins at a young age; the average age at onset was in the early teens. Most of the subjects in this sample were female (the female-to-male ratio was 15:1), supporting the impression from the literature that hair pulling is more common in females (3, 4, 7). The magnitude of this ratio may have been exaggerated by a number of factors. The smaller number of male subjects in the study group may reflect a lesser tendency for men to seek help for trichotillomania. Hair pulling more frequently occurs over the vertex of the scalp, a pattern similar to male-pattern baldness, and this may provide a natural "disguise" for the male hair puller. Natural balding might similarly limit the hair available for pulling in this region. One study (6) noted that hair pulling by males involved the beard and moustache (only 40% of the males pulled out scalp hair), and such a pattern might provide an opportunity for males to prevent hair pulling by shaving these areas. One of our male subjects described such behavior.

Seventeen percent of the subjects denied experiencing either mounting tension before pulling out hair or gratification or relief after pulling out hair and did not meet the *DSM-III-R* criteria for a diagnosis of trichotillomania. It is interesting that these characteristics were often absent for one or more of several hair types pulled; perhaps as hair pulling generalizes to involve several hair types, the tension-reduction qualities of the behavior are reduced or lost. All subjects acknowledged either tension before or gratification after some hair pulling, suggesting that mounting tension or relief is important in the maintenance of some of their behavior; however, *DSM-III-R*'s requirement that both must be present for the diagnosis of trichotillomania may be overly restrictive.

It was expected that most subjects would pull out hair with the dominant hand. It was surprising, then, to find that of the subjects who reported the hand that they used to pull hair, equal numbers identified the dominant and the nondominant hands. This suggests that in a subgroup of hair pullers who use the nondominant hand, hair pulling occurs while the dominant hand engages in another primary activity, such as writing, and may indicate lack of attention to the hair-pulling behavior.

Trichotillomania is associated with other psychiatric conditions. Our study sample had a greater lifetime prevalence of anxiety, affective, and addictive disorders than has been noted in the general population (14), as well as frequent comorbid eating disorders. The high rate of mood disorders and other disorders in the so-called affective spectrum (obsessive-compulsive disorder, panic disorder, eating disorders) suggests that trichotillomania may be a variant of depression. This postulation is, of course, based on information obtained from a semistructured interview, which is less comprehensive than a structured interview, and it is made without a comparison of the subjects to matched normal control subjects. The Minnesota Trichotillomania Assessment Inventory also required that the interviewer have a working knowledge of *DSM-III-R* diagnoses, which were assigned apart from data from the instrument. Incorporation of established structured interviews such as the Structured Clinical Interview for DSM-III-R (15) in future studies of hair pullers would help overcome these limitations. The greater prevalence of psychiatric disorders that we found may also have been an artifact of sampling, as individuals who present to a trichotillomania clinic or for participation in a study may be more psychiatrically disabled; people whose problems are limited to hair pulling may be less likely to seek help.

The high prevalence of other psychiatric disorders raises the question of whether trichotillomania is a separate psychiatric disorder or whether it is a symptom of other psychiatric illness. The high prevalence of other habits in our sample suggests that hair pulling might represent only one method of tension relief in psychiatrically disabled individuals. Several investigators view hair pulling as similar to other habits such as nail biting and thumb sucking (4, 7, 8). Without comparison to control subjects, however, it is unclear whether these habits are associated with trichotillomania and psychiatric disability or whether they are common in the general population.

Several investigators have suggested that trichotillomania may be a variant of obsessive-compulsive disorder (13, 16). If this were true, one would expect a higher incidence of other obsessions or compulsions in persons with trichotillomania, as most patients with obsessive-compulsive disorder do not have just one obsession or compulsion. One study (17) noted that 60% of 44 patients with obsessive-compulsive disorder had multiple obsessions. Thirty-three percent of our subjects reported obsessions and/or compulsions, although only 15% fulfilled the criteria for current or past obsessive-compulsive disorder. This percentage is higher than one would expect in the general population (14) but lower than one might predict if trichotillomania were a variant of obsessive-compulsive disorder. It is unlikely that use of the Minnesota Trichotillomania Assessment Inventory resulted in underreporting of obsessive-compulsive symptoms, as the instrument screened for 10 obsessions and 10 compulsions common in obsessive-compulsive disorder (18). The observation that only 15% of the subjects said that they are always fully aware of their hair pulling and that it is the primary focus of their attention is further indication that trichotillomania is not a form of obsessive-compulsive disorder. This lack of full awareness contrasts with the purposeful quality ascribed to compulsions. Finally, an equal ratio of males to females is found in obsessive-compulsive disorder but not in trichotillomania. Evidence supporting a connection between the two disorders includes the response of trichotillomania to treatment with the antiobsessional drugs fluoxetine (13, 19) and clomipramine (13). Clomipramine was shown to be superior to desipramine in a double-blind crossover study (13), suggesting that clomipramine has a specific antitrichotillomanic effect as opposed to a benefit exclusively due to its antidepressive qualities. This observation suggests that trichotillomania is not merely a variant of affective disorder as its association with other disorders might indicate.

Trichotillomania appears to be more common than previously expected, as evidenced by the availability of a large sample of subjects. In adulthood the disorder follows a chronic course, frequently involves multiple hair sites, and is associated with high rates of psychiatric comorbidity. Further research into the phenomenology, etiology, and treatment of this disorder is indicated.

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Nortriptyline Treatment of Depressed Cardiac Transplant Recipients

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The safety of tricyclic antidepressants in cardiac transplant recipients has not been established. The author used nortriptyline to treat major depressive episodes in eight cardiac transplant recipients. Nortriptyline therapy was associated with increased QRS interval and heart rate but did not significantly affect other hemodynamic or ECG variables or cyclosporine dose requirements. It appears that nortriptyline may be used safely in depressed cardiac transplant patients.

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Patients who have received heart transplants are returning to the community. More than 9,100 heart transplant operations have been performed in the United States, mostly in the last 5 years. Improvements in surgical and postsurgical management, especially the introduction of the immunosuppressive agent cyclosporine in 1980, have led to greatly enhanced survival of heart transplant recipients: the 1-year survival rate now exceeds 80%, and the 5-year survival rate is about 74% (1). The improved survival and increasing number of operations performed have led to observations of long-term psychiatric sequelae in heart transplant recipients. These observations have shown that affective disorders are highly prevalent in the post-transplant lifetime experience of heart recipients (2–5). This consistent finding may be attributed in part to the side effects of steroid drugs included in the immunosuppressive regimen, in part to the stresses associated with being a heart transplant patient, and in part to the other vicissitudes of the patients' lives. In any case, it implies a substantial need for safe and effective treatment. Because of the denervation of the transplanted heart, special concerns apply.

The use of tricyclic antidepressants to treat depression is routinely complicated by cardiovascular and other side effects. These include anticholinergic effects, orthostatic hypotension, and disturbances of cardiac conduction. Although early fears that tricyclic drugs were arrhythmogenic at therapeutic doses have been shown to be erroneous (6), it remains clear that they may prolong conduction through the His-ventricular portion of the cardiac conduction system, resulting in prolongation of the PR interval, and through the ventricular conduction system, with potential for first-, second-, or third-degree atrioventricular block and bundle branch block, dropped beats, or complete heart block. Similarly, earlier reports that reduction of cardiac output and left ventricular ejection fraction may be of concern in patients with cardiac failure have been found to be flawed, and subsequent reports have shown that left ventricular function is not impaired by tricyclic antidepressants, even in patients with cardiac failure. However, orthostatic hypotension is an important clinical problem for heart failure patients treated with some tricyclic antidepressants such as imipramine. The use of nortriptyline has been associated with

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TABLE 1. Cardiovascular Effects of Nortriptyline in Eight Heart Transplant Patients

	Baseline		During Nortriptyline Treatment		Paired t Test		
Measure	Mean	SD	Mean	SD	t	df	p
Heart rate (bpm)	94	10	106	5	−2.69	7	0.03
Cardiac output (liters/min)	5.96	1.60	5.49	1.70	1.40	6	0.21
Blood pressure (mm Hg)							
Supine							
Systolic	136	22	139	21	−0.37	7	0.73
Diastolic	91	13	101	19	−1.73	6	0.13
Upright							
Systolic	128	25	131	31	−0.23	3	0.83
Diastolic	97	22	101	24	−0.33	3	0.76
ECG Intervals (msec)							
PR	148	31	144	26	0.26	6	0.804
QRS	91	18	108	18	−4.07	6	0.007
QT	344	18	319	30	1.81	6	0.120
QTc	394	40	436	50	−1.09	4	0.339

much less risk of substantial orthostatic hypotension (7, 8).

Although some previous reports (2–4) referred to treatment of depressed heart transplant recipients, no specific information was given. Since cardiac transplant recipients have no autonomic innervation to their new hearts, they are physiologically distinctive, lacking both vagal effects, such as slowing of sinus nodal rhythm and conduction through the atrioventricular node, and sympathetic effects, including increasing heart rate and contractility. The effects of tricyclics on the denervated human heart are unknown. Because nortriptyline has been reported to cause relatively little orthostatic hypotension and to be safe for use in patients with impaired left ventricular function (7), it seemed plausible that it could be used to treat depressed heart transplant recipients. This paper reports the cardiovascular and other pertinent effects of nortriptyline in eight heart transplant recipients.

METHOD

The Presbyterian Hospital has had an active heart transplantation program for the past 10 years. Of the 360 patients who have received transplants through June 1990, 252 survive. In 1989, 87 heart and heart-lung transplants were performed. All patients are evaluated by a psychiatrist as part of their preoperative evaluation and followed postoperatively while hospitalized. After discharge, patients are seen on an as-needed basis by self-referral or referral from the transplant service cardiologists. All patients routinely undergo periodic right heart catheterization and endomyocardial biopsy to monitor signs of organ rejection; during the catheterization, cardiac output is determined by standard thermodilution techniques. Cyclosporine dose is titrated frequently, guided by determination of serum level.

Nine patients have been treated with nortriptyline since June 1986. Eight were men. Their mean age at the time of transplantation was 45 years (range=26–60). Six were white, two Hispanic, and one black. For five patients the original cardiac diagnosis was ischemic heart disease due to atherosclerotic coronary artery disease; four patients had the diagnosis of cardiomyopathy. One patient had a pretransplant history of major depressive disorder. For all nine, the indication for antidepressant treatment was a major depressive episode meeting *DSM-III* criteria. The patients began nortriptyline therapy 2–18 months after transplantation.

One patient complained of intolerable sedation on only 25 mg/day of nortriptyline, requiring termination of the drug trial, despite a low blood level of the drug. The other eight patients all achieved a blood level of 50–150 ng/ml. The mean nortriptyline level achieved was 95 ng/dl (range=56–131). The mean nortriptyline dose was 96 mg/day (range=40–200). Seven of the patients showed clinical improvement; one patient, whose treatment occurred while critically ill, died of sepsis without obtaining a clear-cut antidepressant effect. The results presented later in the paper pertain to the eight patients for whom therapeutic blood levels of nortriptyline were obtained.

The following measures were routinely obtained serially throughout the treatment of the patients given nortriptyline: ECG, heart rate, systolic blood pressure and diastolic blood pressure while supine or sitting and while standing, and serum nortriptyline level.

Values obtained at baseline and after a therapeutic nortriptyline level (9) was obtained were compared by using paired t tests (two-tailed) to determine the effect of nortriptyline treatment on cardiovascular function and cyclosporine therapy.

RESULTS

The cardiovascular effects of nortriptyline on the eight transplant recipients are summarized in table 1. There were no significant effects on blood pressure, and no patient developed orthostatic hypotension. The patients' mean heart rate and their mean QRS interval increased significantly (see table 1). Changes in the PR, QT, and QTc intervals, however, were not significant. Two patients developed intraventricular conduction delay or incomplete right bundle branch block pattern, but no patient developed even first-degree atrioventricular block. All of the cardiovascular effects observed were well tolerated and regarded by the cardiologists as of no clinical significance.

Cyclosporine levels were held in a therapeutic range by frequent dose adjustment according to blood level determinations. Cyclosporine levels fell by 8% from a baseline mean of 216±124 ng/dl to 198±67 ng/dl during nortriptyline therapy (t=0.37, df=7, p=0.725). The cyclosporine doses, however, fell by 35%, from a baseline mean requirement of 638±312 mg/day to 416±228 mg/day (t=1.67, df=7, p=0.139). This suggests that nortriptyline may actually tend to raise the plasma level of cyclosporine.

DISCUSSION

Several limitations of the study should be acknowledged. First, these findings are based on the study of eight patients, a small sample. The power of so small a sample to demonstrate significant treatment side effects is limited. Second, these patients were not in heart failure. Nortriptyline has been shown to be relatively safe for patients with heart disease and left ventricular dysfunction (7, 8), and this finding may also hold for heart transplant recipients with left ventricular failure, but this remains to be demonstrated. The findings of this study are not intended to be generalized to heart transplant recipients with left ventricular impairment. Third, this study used cardiac output, measured during routinely obtained right heart catheterizations, as its measure of cardiac function. This is not directly comparable to a measure of ventricular function such as the left ventricular ejection fraction determined by radionuclide scan, which was used in the study of Roose et al. (7). However, since the present study was limited to observation of treatment effects, and since there was no clinical indication to obtain ejection fraction measures in these patients, such data were not available.

Although these results should be viewed with appropriate caution, it does appear that nortriptyline is well tolerated by heart transplant recipients. Nortriptyline appears to have little clinically significant effect on heart rate, blood pressure, cardiac output, or ECG pattern. Cyclosporine immunosuppressive therapy was not complicated by the addition of nortriptyline, but the precise effect of nortriptyline on cyclosporine levels needs further evaluation, and cyclosporine levels should be followed closely during induction of nortriptyline treatment. Nortriptyline use was well accepted by the patients and the cardiologists. Given the prolongation of QRS interval seen in this small series of patients, cautious monitoring seems indicated in trials of nortriptyline for heart transplant patients with preexisting conduction disturbances or heart failure.

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Transdermal Nicotine and Smoking Behavior in Psychiatric Patients

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The authors used a double-blind crossover design to observe the effect of transdermally administered nicotine on the smoking behavior of 13 psychiatric patients who were not trying to stop smoking. The patients smoked significantly fewer cigarettes while receiving nicotine than while receiving placebo. These data suggest that transdermally administered nicotine can be a useful adjunct in treating nicotine-addicted psychiatric patients in a non-smoking environment.

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Cigarette smoking, which is addictive and health damaging (1), is especially prevalent among psychiatric patients (2). As more psychiatric facilities limit smoking in order to reduce smokers' morbidity and nonsmokers' exposure to secondhand smoke (3), cigarette consumption will become increasingly troublesome. Smoking cessation programs, especially those incorporating behavioral techniques and nicotine chewing gum, have had an impressive impact on short-term smoking rates in nonpsychiatric subjects (1, 4, 5). However, little work has focused on developing or implementing interventions for psychiatric patients. Impediments to designing successful smoking cessation programs for psychiatric patients may include less desire to quit smoking and impaired cognitive functioning, which may preclude following detailed instructions regarding techniques such as self-monitoring and appropriate use of nicotine gum. Therefore, for psychiatric patients in a smoke-free hospital setting, reduction of nicotine withdrawal symptoms by means of a technique that does not require strong motivation to quit or the need to follow complicated instructions might be extremely useful. Moreover, such a technique might yield greater smoking cessation rates for motivated individuals with higher levels of cognitive functioning.

Transdermal nicotine administration has shown promising preliminary results in reducing smoking rates (6–8). This technique may have special benefits for psychiatric patients because it is uncomplicated and appears to have an impact on smoking even among individuals who have expressed little desire to quit. The pilot study reported here was designed to ascertain whether transdermal nicotine administration would reduce the number of cigarettes smoked by a group of psychiatric patients.

METHOD

We obtained informed consent from 14 competent men (three inpatients and 11 outpatients) who were voluntarily receiving psychiatric services, smoked at least 10 cigarettes per day, were free of substantial cardiovascular and pulmonary disease, and did not have a current substance use disorder. Patients did not have to indicate any desire to quit smoking and were given $10 in coupons redeemable at the hospital canteen for participating in the study. Four of the patients were white, seven black, two Asian, and one Hispanic. They reported smoking an average of 22.9 cigarettes per day (range=10–30) and had been smoking for 19.0 years (range=9–44). Their mean age was 40.9 years (range=31–59).

A double-blind, within-subjects crossover design was used. Patients were randomly assigned to receiving 24 μl of a solution containing either 30% nicotine base (8 mg) or water (placebo) applied to the nondominant forearm during session 1 and receiving the other solution during session 2 one week later. Each solution was covered by a 3-cm square patch of polyethylene wrap secured at the edges by surgical tape. The solutions were applied at 10:00 a.m., and patients were provided with unlimited access to their preferred brand of cigarettes for the next 7 hours. To maintain the double-blind design, the investigator responsible for ran-

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TABLE 1. Number of Cigarettes Smoked by 13 Psychiatric Patients While Wearing Patch of Transdermal Nicotine or Placebo

Subject	Diagnosis	Nicotine[a]	Placebo
1	Organic mental disorder	7	5
2	Schizophrenia	10	9
3	Schizophrenia	11	11
4	Schizophrenia	14	18
5	Major depression	7	6
6	Schizophrenia	7	12
7	Schizophrenia	15	20
8	Schizoaffective disorder	8	12
9	Schizoaffective disorder	12	13
10	Schizophrenia	7	11
11	Schizophrenia	11	10
12	Bipolar disorder	10	12
13	Schizophrenia	10	14

[a] Subjects 1–8 received the nicotine patch in session 1; subjects 9–13 received it in session 2.

dom assignment (N.H.) had no further contact with patients during the sessions. The patients were told that the patch might influence smoking behavior, to try and ignore the patch, and to smoke as they normally would during the session and during the week between sessions. They spent the entire 2 days in the clinic, where lunch and entertainment (video movies and board games) were provided so that study personnel could observe them at all times and ensure that each patient collected his cigarettes in his own container.

RESULTS

The results for the 13 patients completing the protocol are given in table 1. A repeated measures analysis of variance with number of butts collected after session 1 and session 2 as the dependent variable revealed no significant effect of repeated experimental sessions (F=0.03, df=1, 11, n.s.) or for order of patch wearing (F=0.02, df=1, 11, n.s.) but did indicate a significant interaction between session and order of patch wearing (F=5.84, df=1, 11, $p<0.04$). This interaction indicates that participants smoked significantly less while wearing the nicotine patch (mean±SD=9.9±2.7) than while wearing the placebo patch (11.8±4.1).

Table 1 also reveals that only patients who smoked at least 12 cigarettes (approximately 1.8/hour) while wearing the placebo patch achieved benefit from the nicotine patch, suggesting that the patch was more effective with heavier smokers. On questioning, no patient reported any difference in his subjective experience while wearing the two patches (irritation at the patch site, taste, smell), nor did either the patients or the observers note any alterations in the patients' clinical status.

DISCUSSION

Wearing a nicotine patch yielded a moderate but statistically significant reduction in the number of cigarettes smoked among a group of psychiatric patients who were long-term smokers. Importantly, this effect seemed independent of the patient's active interest in giving up smoking or cognitive awareness. This factor may become especially important as more psychiatric facilities convert to smoke-free environments (9).

Patients who smoked more cigarettes while wearing the placebo patch (who might be both more strongly addicted to nicotine and at greater risk for smoking-related physical morbidity) achieved a greater reduction in the number of cigarettes smoked while wearing the nicotine patch. In fact, none who smoked fewer than 12 cigarettes while wearing the placebo patch smoked fewer cigarettes while wearing the nicotine patch. Among the subgroup of heavier smokers, cigarette consumption was reduced 24% when patients wore the nicotine rather than the placebo patch.

Two provisos must be kept in mind when viewing these results. First, our finding that the heavier smokers appeared to benefit more is in contrast to at least one study of nonpsychiatric patients, which found that lighter smokers benefitted more (8). Second, we have not ruled out the possibility of a change in smoking topography so that even as the number of cigarettes consumed decreased, the amount of nicotine may not. For example, subjects may have increased the depth of their smoke inhalation or covered their cigarette filter with their fingers to increase the smoke they inhaled and thus absorbed more nicotine. Nonetheless, the data suggest that transdermally administered nicotine can be a useful adjunct in maintaining nicotine-addicted psychiatric patients whether or not they want to stop smoking permanently.

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Book Forum

Nancy C. Andreasen, M.D., Ph.D., Editor

PSYCHOANALYSIS

The Empathic Imagination, *by Alfred Margulies. New York, W.W. Norton & Co., 1989, 172 pp., $22.95.*

Early psychoanalysis had a special commitment to the belief in the power of rational enlightenment. An essential constituent of Freud's program was the notion that scientific insight would lead to social reform and, in the long run, amelioration of human suffering. So Freud challenged traditional family customs and sought to free people from superstitions and illusions. Throughout Freud's career he retained the ambitions of a social prophet; as a therapist, however, he also sought to rely on the efficacy of insight. Through reconstructing the patient's early years by means of the analyst's relying on the technique of free association, Freud thought that patients could gain a key leverage over the past and be able to make more rational choices.

Freud sought to structure his theories so that they would form a body of knowledge which would fulfill the standards of scientific theory; he thought not only that his findings were capable of being verified but that he and his followers had brought solid evidence to support his hypotheses. In practice, Freud had considerable artistic powers and ranks as the greatest writer among twentieth-century psychologists. But he distrusted his own capacities for art and presented his conclusions as a scientific system. It was in this sort of rationalistic mood that Freud was capable of criticizing intuition as an illusion, a form of hocus-pocus produced by the need for wish fulfillment.

Freud's critics within modern psychotherapy were unhappy with this aspect of his approach; they thought that much more had to be involved in helping patients than simply the analyst's offering them rational insight. Furthermore, critics often said that old-fashioned suggestion lay hidden behind the supposed neutrality of Freud's approach. By now there is some agreement that the whole conception of psychoanalysis as the quest for abstract truth implied that the analyst was capable of being ideally rational and that the patient was susceptible to all kinds of infantile strivings. Therefore, Freud wrote about the existence and significance of the patient's emotional transferences, whereas he treated the analyst's countertransferences as a potential interference in the laboratory-like clinical situations he believed he had created.

More recently, Freud's school of thought has been moving away from his own most scientific-sounding pretensions, and many of the points that his critics tried to establish are now being accepted in psychoanalysis. Alfred Margulies's book is a touching and concrete account of a modern psychoanalyst's trying to come to terms with the demands of a clinical practice conducted with a humanistic orientation. Margulies is searching for light on the problem of empathy without making an effort explicitly to challenge the earlier psychoanalytic premium on insight. Margulies's outlook points to more of a burden on the therapist, since in principle the therapist, incapable of being omniscient, is only a working partner in an inherently troubled alliance with the patient struggling for help.

The result is that *The Empathic Imagination* relies on a broad range of sources. Margulies has broken with past sectarian orthodoxies and feels free to cite some of the ideas of Carl Jung, Otto Rank, Karen Horney, and Harry Stack Sullivan when he finds them relevant. Although Freud thought that psychoanalysis was capable of avoiding the traditional problems of philosophy, Margulies rightly tries to confront some of the central dilemmas of moral thought; he makes the whole problem of "world view" a central one clinically. And he is willing to tell us about at least one clinical occasion when he felt secure in prescribing a drug like lithium, in contrast to an earlier generation of analysts who frowned on using medication.

The self psychology of Heinz Kohut has been centrally responsible for a shift in psychoanalytic thinking over the last two decades, and Margulies—without being doctrinaire about it—relies on Kohutian terminology. Margulies is more catholic than most analysts in the thinkers he relies on, but I believe that he might benefit from going back to the concept of a phenomenological self advanced by the early analyst Paul Federn. The work of Erik Erikson, although touched on in passing in this book, is also more unfashionable currently than it deserves to be for those eager to move in the general direction of emancipating analytic thinking from the constraints of scientific reasoning.

Apart from all theoretical issues, Margulies is centrally concerned with the various functions of psychotherapy and how personality changes can be mobilized. Yet here I wonder whether he unwittingly is not too tied to past orthodox techniques. For example, he presents us with an extended account of one of his cases, an apparently regressed woman who has trouble coming to terms with Margulies's office renovations. But only in passing does Margulies mention his silences and the use of the couch. It is hard for me not to wonder to what extent his patient was reacting not so much to the exigencies of her own psychopathology as to the emotional deprivation of the setting of the classic analytic situation itself.

Margulies tells us how important in his own training was the example of the Boston psychiatrist Elvin Semrad and how Semrad concentrated on the analyst's special supportive functions. As a student, like Margulies, I also "experienced Semrad as magical," but I think it is time to try to decipher where even someone as extremely talented as Semrad might have been hobbled by the constraints of the theoretical concepts of his psychoanalytic era. Margulies has succeeded in going far beyond the conventional pieties that used to be customary at our best psychoanalytic training centers, but my impression is that if he continues along the road he has chosen he will find that others before him, even if they have not recently been fashionable to cite, have seen some of the main inadequacies of the excessive rationalism that we owe to early psychoanalytic thought.

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Understanding Countertransference: From Projective Identification to Empathy, *by Michael J. Tansey and Walter F. Burke. Hillsdale, N.J., Analytic Press, 1989, 222 pp., $27.50.*

Despite economic pressures exerted by a "quick fix" ethos, times are good for psychoanalytic psychotherapists. The last two decades have witnessed a revolution in psychoanalytic theorizing (1). These developments have stimulated a rich, abundant, and rapidly evolving clinical literature. The decline of mechanistic models of human nature (2), the clinical conceptualization of "experience-near" (3), application of research paradigms to psychotherapy (4), and the "manualization" of technique (5) have done much to demystify what the psychoanalytic psychotherapist does, how he or she goes about it, and what is most effective.

This slim volume, coauthored by two Chicago psychologists, maintains that psychoanalytic psychotherapy "is a radically mutual process fully involving two individuals who exert a mutual and ongoing influence upon one another" (p. 4). Tansey and Burke conceptualize projective identification, countertransference, and empathy, traditionally considered separately, as integrally related aspects of patient and therapist intersubjectivity.

Projective identification represents the patient's efforts—conscious and unconscious—to induce in the therapist various affects and role responses. Countertransference is the therapist's subjective response to these interactional pressures, a blend of both patient-evoked responses and experiences deriving from the therapist's unresolved biographical and psychological conflicts. Following Sandler (6), the authors emphasize the "compromise existing between the therapist's unique personality makeup and the patient's capacity to infuse the therapeutic relationship with his own particular wishes and needs" (p. 41). The strength and nature of these patient-induced self-experiences may at times be quite painful to tolerate, provoking nonproductive therapist responses. Empathy represents the desirable outcome of processing projective identifications into sources of awareness and understanding.

After defining their terms and providing a brief historical overview, Tansey and Burke propose "a schema for analyzing the therapist's identificatory experience" (p. 37) as it emerges in the clinical interaction. Their model encompasses four sequential phases, at any point of which the therapist may be derailed in the effort to understand the patient's communications. The phases include 1) reception (receiving and experiencing the particular sense of self evoked by the patient's projective identifications), 2) internal processing (tolerating and considering internal reactions and evaluating their potential for intervention), 3) communication (encompassing assessment and implementation of interventions), and 4) validation (ongoing evaluation of the validity of the therapist's reactions and responses). The model of validation offers a particularly useful approach for accepting or discarding clinical hunches and addresses what the authors consider a most controversial topic, namely, the "use" of countertransference (to disclose or not to disclose, that is the question).

Aside from the lucidity of the presentation, a particular value of *Understanding Countertransference* is that it readily brings to mind, with vivid perspective, interactions with one's own patients. As applied object relations theory, *Understanding Countertransference* bridges clinical theory and practice. It has special value for psychotherapy supervisors, providing guidelines for the management of difficult countertransference experiences and strategies for untangling miscommunications, blunders, and impasses that bedevil all psychotherapists, especially those in training. Accessible, practical, and theoretically sophisticated, *Understanding Countertransference* makes an important contribution to the prime directive of psychoanalytic psychotherapy: growth through self-understanding.

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Transformations: Cross-Dressers and Those Who Love Them, *by Mariette Pathy Allen. New York, E.P. Dutton, 1989, 160 pp., $24.95.*

This is a remarkable book of interviews and photographs. Cross-dressers, who make up between 3% and 5% of the male population of the United States, come from all occupations, including medicine, and from all levels of society and all racial groups. The majority are heterosexual. These are husbands, fathers, and grandfathers who have needed to express themselves, at least part of the time, in the roles and clothes of women. Often the cross-dresser considers this the most important part of himself, emotionally. Understanding of this group may help us to better appreciate the human possibilities that might follow from a better balance or synthesis of the characteristics that are culturally (at least) perceived as feminine and masculine. This book would enlarge the insights of psychiatrists into human sexuality as well as enhance their aesthetic experience.

The photographs by the author are extraordinary. Allen is a true artist who captures, for example, a cross-dresser playing with his daughter, another cross-dresser engaged in erotic play with his wife. These great pictures are in both black and white and in color. Police officers, a Navy man, an ex-Green Beret, an aviator, an inventor, and a financial analyst, among others, are portrayed in both everyday clothes and in the glorious clothes beloved by cross-dressers. Allen's work has been widely exhibited in the United States and abroad. You are shocked and haunted as she brings you beyond the boundaries of gender. The key to her photographic success is her empathy.

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Self Psychology: Comparisons and Contrasts, *edited by Douglas W. Detrick and Susan P. Detrick. Hillsdale, N.J., Analytic Press, 1989, 485 pp., $49.95.*

This book presents a broad view of the development of psychodynamic and psychoanalytic theories that one must have in order to be more than a technician, and it goes a long way toward helping the reader recognize that integrating what we know is the task at hand. We are no closer to an integrated field theory in psychiatry than we are in physics. I hear more scientists and practitioners in psychiatry speaking this way. Let me suggest you read the title of this almost 500-page book carefully. It is not about self psychology alone.

The editors begin their task of integration by emphasizing the overlap in seemingly independent systems of thought and referencing the relatively unheralded explosion in developmental and dynamic research. They discuss drive theory, object relations, ego psychology, and self psychology in a fashion that places them in historical context and in current theoretical and technical terms. In this way we see some of the cyclical patterns. Ferenczi, Alexander, French, and others were straining at some rigid views of psychotherapy when drive theory was predominant, being interpreted dogmatically, and at odds with some clinical observations. A more humanistic view was being advocated. In this climate, existentialism and humanism gained momentum in the psychiatric community, and ego psychology became a more coherent body of knowledge describing many new clinical observations in evocative detail. Object relations evolved in a similar fashion and so did self psychology. These theories did not arise de novo from a genius or two. They are the results of continuing observation, experimentation, and communication within the scientific community. How else could ideas be widely accepted and organized? There is a chapter on the philosophy of science that speaks to this issue, but it is also addressed frequently (although indirectly), as it must be in a book of this scope.

Arnold Goldberg mentions in the foreword that it is easy to find bones to pick with the many contributors; in fact, this may be a key to fully appreciating this work. Goldberg says, "I rediscovered a feeling that has not commonly accompanied my usual reading: it is simply that I wanted to talk directly to the author" (p. xvii). I experienced similar feelings. In contrast to an overview text, this work is best suited to those familiar with the topics. The summaries of theories such as Mahler's and Kohut's are too brief to offer more than illustrations of the authors' views. The book is written by clinicians who describe the way they think and organize their work. It is very evocative. How many of us in practice find we can rigidly adhere to one school of thought or technical stance? Still, we know that a substantial body of research correlates success in therapy with a coherent view of the problem. The authors help us deal with this apparent dilemma.

Michael Basch begins, in chapter one, with his view of Freud, psychoanalysis, and Kohut. He concludes, "Self psychology is not a separate or new form of psychotherapy but is very much an extension of and a corrective for traditional psychoanalytic practice . . . . Self psychology will be seen as the evolutionary successor to ego psychology" (p. 20). It is fascinating to follow his logic and stimulating to recognize what you disagree with. Where, for example, does Basch place object relations theorists? Could he elaborate on how he synthesizes everything under the rubric of self psychology? I wish he had written more, but this is the strength of the book: scholarly, educational, thought-provoking, brief, personal presentations that leave you hungry for more. The contributions of Jung, Adler, Rank, Ferenczi, Horney, Rogers, Klein, Balint, Fairbairn, Winnicott, Masterson, Kernberg, Lacan, Mahler, and others are discussed in separate chapters. The history of modern psychodynamics comes alive. It is very hard to be an acolyte with such a view. "If self psychology is a novel professional discipline offering a new brand of psychotherapy, I have nothing to say about it, just as I have nothing to say about its countless competitors in the clinical marketplace" (p. 417), writes John Gedo. He believes Kohut's warning would be "not to congeal his writings into self psychological dogma . . . . The attempted reconstruction of a finished theoretical system threatens to obscure his valuable clinical discoveries" (p. 419).

Find a comfortable spot, pick up this book, and enjoy. It may remind you of what attracted you to the field. Whatever, you cannot afford to be ignorant of the topics discussed.

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Exiles From Eden: Psychotherapy From an Evolutionary Perspective, *by Kalman Glantz and John K. Pearce. New York, W.W. Norton & Co., 1989, 308 pp., $32.95.*

This is a groundbreaking attempt at placing psychotherapy within an evolutionary framework. It is written by a student of evolutionary biology studying psychotherapy and a senior psychotherapist who has worked for many years with families. Together they set out to explore evolutionary biology for possible paradigm shifts in psychotherapeutic theory and intervention. They take the reader on an interesting trip through the hunter-gatherer origins of our behavior and emotions and present clinical examples of contemporary therapeutic interactions to highlight the journey. The style is relaxed and informal.

The book starts with an informed overview of sociobiology, with discussions of the contributions of Wilson, Trivers, Gould, and many anthropological observers. Glantz and Pearce emphasize inclusive fitness, which includes cooperation, altruism, and even self-sacrifice as part of a reproductive strategy. (Copies of genes can be transmitted generationally through one's own reproduction *or* that of relatives. The idea of inclusive fitness contrasts with that of the social Darwinists, who see "Nature red in tooth and claw" and "fit" as including only those competitive and ruthless factors leading to personal reproductive success.) The authors' views also deviate from those of psychoanalysis. They argue against the concepts that designate as psychopathology much of what was hardened into our brains and glands as hunter-gatherers perhaps more than 100,000 years ago.

The book presents an excellent broad-brush view of the sociobiological position regarding "strategies" for reproductive success. The authors discuss the psychosocial components that function as enabling mechanisms for such success within the hunter-gatherer band and contrast the "natural" environment of such bands with those of the modern world. Because our brains have not changed as much as our environment, there is an inevitable clash that is often brought to the psychotherapist. By use of clinical examples, the authors illustrate the ways in which understanding of phylogenesis can empower the therapist and help the patient. Other chapters address child-rearing practices among contemporary hunter-gatherers (as an indicator of the social environment from which we are all derived), concluding that accepted child-rearing practices may be damaging to children because of lack of congruence with the way in which we are made. The issues of sex and gender are generously explored, with many clinical vignettes illustrating the problem of our ancient brain in the modern setting, the conflict of moral and religious attitudes with our nucleic acids, and some almost respectful but provocative views regarding female liberation.

A further chapter on "model building" in the human brain presents the views that the modern social scene is too complex for brains set for coping within a hunter clan and that contemporary environments are often in conflict with those enabling forces which led to our antediluvian dominance. The view is advanced that problems in living do not derive (as some biologists claim) from defective circuitry (for every crooked thought a crooked molecule), but that a perfectly good brain can produce a bad model, a model which does not cope with the demand characteristics of the environment. The genetic traits derived from success in our earliest beginnings (we are, after all, still around to write about it) do not always work well; "achievement in . . . one setting [occasions] disability and distress in another" (1). The "natural man," at peace with himself and his environment, resides, in this conceptualization, among the Kung or Mbuti rather than in Boston or Boise. The authors, in a later chapter, contrast their school of psychotherapy with the present schools from within the evolutionary frame. An eclectic and accepting approach is recommended for conceptualizing clinical problems. Final chapters use further illustrations from case material demonstrating the use of information exchange regarding our deepest origins.

This is an expository and occasionally messianic book; its shibboleths call for the most basic revision of psychological understanding. Glantz and Pearce argue, often persuasively, that the unseen hand which guides us is not that of repressed wishes from childhood but, rather, our legacy from a distant past irretrievable by means of subjective reminiscence.

The clinical vignettes presented as illustrative do not always highlight the concepts as intended, and more than a few readers will feel jarred by the style presented by the therapist (direct, confrontative, argumentative, directive, and, at times, sarcastic), but that is often the problem with clinical vignettes: it is difficult to condense therapeutic interchange without losing context and texture. Some of the applications of biological evolution are arguable, and the romaticization of "natural man" as hunter-gatherer may seem old hat; yet this volume can help reshape at least some long-held views of therapists. The book is most informative, is easy to read, and opens the curtain still further on an idea that deserves serious consideration. The first three chapters alone are well worth the price of admission.

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Moments of Engagement: Intimate Psychotherapy in a Technological Age, *by Peter D. Kramer. New York, W.W. Norton & Co., 1989, 266 pp., $24.95.*

Popular books by psychoanalysts designed to inform the educated public have had an important place in establishing communication between the profession and those most likely to use analytic psychotherapy. Kubie (1), Horney (2), and, more recently, Lichtenberg (3) have all chosen to write about psychotherapy and neurosis in a fashion that allows the reader to identify what is neurotic in himself or herself and what form of analytic psychotherapy is to be expected. Peter Kramer breaks new ground by writing a book that is designed to inform the reader about psychotherapy by revealing the way in which the author sees himself thinking while he is conducting psychotherapy. By detailing aspects of his inner life that appear while he is working clinically, Kramer hopes the reader will "make sense of the ways in which those who deal with problems of mind daily think about the mind now." Kramer writes about his emotional responses to clinical experiences that he has had during medical school, residency, and in the private practice of psychotherapy.

Despite the author's lively, informal, journalistic style (he writes a regular column in *The Psychiatric Times*), the psychiatric reader is likely to experience a mixed response to his self-laudatory tone. Kramer's premise—that a review of how he works will illustrate how a modern psychotherapist works—reflects a high degree of self-centeredness. Furthermore, much of the text is devoted to a variety of clinical examples that involve interactions and interventions that many clinicians would find open to question as to their meaning and effectiveness. By placing such great emphasis on himself, Kramer implies that the value of the book should be drawn from an evaluation of his version of how he developed as a psychiatrist and what kind of psychiatry he currently practices. Thus he unintentionally opens himself to scrutiny of unresolved problems in his development as a psychiatrist.

Dynamically oriented individual psychotherapists might find it easy to disavow Kramer's description of himself as psychoanalytically oriented. Many family therapists as well as psychopharmacologists might also distance themselves from his description of how he applies their approaches. Most of Kramer's errors lie in the area of judgment rather than in what techniques he chooses for a particular patient. With one schizophrenic patient, for example, he describes a family intervention that includes massaging the father's neck as a mode of achieving entry into the family system. This choice might be questioned as unnecessary because other modes, such as making a verbal contract, could have been used. In addition, Kramer's subsequent collaboration with the patient in keeping the military unaware of the patient's need for intramuscular fluphenazine on the grounds of confidentiality could hardly be deemed acceptable. Kramer sees his dilemma in this situation in terms that should apply to patients with functional self-observing ego capacities, which certainly was not the case, even when the patient was medicated. With regard to this patient Kramer states,

> He had learned at long last that he needed the shots to function. He had guessed—I had guessed too—that if he asked the army for an antipsychotic, he would be discharged. When he was sent to a base far from here, he asked, what should he do? We decided he should find a civilian doctor off the base and get an injection on his leave time. The military had made the judgment to take him, and I had no intention of interfering with their

> decision. If he stayed with it long enough to move to a sensitive position, to combat duty say, and I knew about it—I would face that day when it arose. For the moment I was grateful to be sworn to confidentiality.

Kramer states that he would face his responsibility when and if a crisis occurred. But what about the risk for the health and safety of such a severely disturbed, medication-dependent patient in the military, not to mention the potential risk to the safety of others if he were suddenly deprived of his medication. What about legal if not clinical responsibility? Finally, why present this example in a positive light when it is actually an excellent example of a countertransference-based error?

This clinical example is one of many used by Kramer to illustrate his ideas of how a modern psychotherapist works. Kramer feels that his mixture of thinking based on many schools of psychological theory plus biological psychiatry represents a new synthesis for the medically trained psychotherapist. He is certainly correct in referring to the many sources of information and theory an alert psychiatrist should be able to draw on. However, he is far too eager to abandon the close scrutiny of dynamics and their interpretation to patients with the capacity to form a working alliance and the observing ego to work with the therapist. The patients in Kramer's practice all seem to him more suitable for manipulations of a variety of sorts; he seems particularly partial, according to the cases he presents, to paradoxical directives, which he delivers to the patient with considerable energy. So much of Kramer's personality shows through in his work with patients that it is difficult not to believe that the force of his personality is a predominant factor in the success of his psychotherapy. Kramer's willingness to show and use his personality in psychotherapy is an advance over the image of the therapist as hidden behind a remote, passive, and so-called neutral facade. However, this forceful personality might be better applied to encouraging the patient's exploration of transference feelings and meanings. The reflection and delay that are essential for the therapist to reflect on countertransference feelings and to use the countertransference in a successful insight-building way are simply not present in Kramer's presentation of himself at work.

There is no question that this memoir reveals a lively personality at work. As such, it manages to dramatize the process of becoming a psychiatrist. It will certainly overcome any image of the psychiatrist as an overly controlled, professionalized personality with such mastery over his or her emotions that the possibility of a human encounter is eliminated. On the other hand, Kramer's excessive exuberance over himself and those training experiences will detract from any accurate image of dynamic psychotherapy that might otherwise be conveyed. It is unfortunate that the author, with his ability to attract attention to psychiatry, failed to be more discerning in describing dynamic psychotherapy as an entity. By equating psychotherapy with all the intuitive interventions that he has chosen or been forced into by practice of general psychiatry, Kramer generalizes beyond the scope of his experience.

This personal memoir captures the experience of one individual's response to the current state of psychiatric training. As such, it will be of interest to those psychiatrists who are interested in issues of training. Kramer's experience, as he relates it, reminds us that the basic personality of the trainee will be a dominant factor in determining which materials of our greatly expanded clinical specialty will be selected, assimilated, and used by the individual who completes psychiatric training. Despite Kramer's interest in and use of many trends within psychoanalysis, psychopharmacology, and family therapy, his personality remains at the center of the clinical work he describes. Kramer's telling of his story, although entertaining, remains more about him than about the current practice of psychotherapy. Psychiatrists will undoubtedly recognize this fact and respond to the personality revealed in the memoir as separate from their understanding of present-day standards of analytic psychotherapy. The book may be more difficult, however, for the nonprofessional reader. The picture of such an informal and direct psychotherapist can dispel some notions of psychiatrists as cold or distant, but it can also encourage resistances to needed and legitimate explorations of the self. Kramer's comfort with taking over for the patient and making manipulative suggestions may be effective and helpful to those individuals who require such interventions. He fails to illustrate or reveal how he would work with patients capable of insight-oriented psychotherapy. The author's pleasure at his own activity, while easily understood, unfortunately has prevented him from distinguishing between what he does himself and the history and literature that determine a generally accurate picture of analytic psychotherapy. Hence, this book must be read for its autobiographical picture of a lively personality rather than as a guide to modern dynamic psychotherapy for either the educated public or the profession.

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CROSS-CULTURAL ISSUES

Mental Health for Refugees and Other Migrants: Social and Preventive Approaches, *by Joseph Westermeyer. Springfield, Ill., Charles C Thomas, 1989, 197 pp., $38.75.*

At a time when biological approaches seem to reign supreme in psychiatric research and practice, it is refreshing to find a book that addresses social issues and calls the reader's attention to the plight of millions of real people. The multitude of mental health problems generated by the flow of refugees and other migrants in different parts of the world makes Westermeyer's book a much-needed contribution. The author's extensive background and experience in the well-known international clinic at the University of Minnesota Department of Psychiatry show well in the broad scope and structure of the book. It could be considered a primer on this subject and, as such, has all the strengths and weaknesses that the reader would expect. Even though the author indicates in the foreword that "refugees have been selected as the primary example of the 'migrant at risk' since they exemplify most of the vulnerabilities manifested by migrants," one gets the impression that, except for the severity variable, this distinction may be irrelevant, not well delineated, or of limited operational value. The migrant's experience appears to trigger such a broad emotional upheaval that an attempt to dissect it meticulously on the basis of the type of migrant may prove to be futile and/or redundant.

The value of the book depends on the reader's perspective or interests. If one is a social psychiatry researcher, the chapter on categories and concepts offers a thorough list of all the variables to be considered in preparing a project or a grant proposal. These include areas ranging from demographic characteristics to victimization and geographic variables. They extend to the changes in attitudes, values, beliefs, mores, recreational activities, communication, cultural conflicts, life cycle, loyalties, and religious practices brought about by migration. The researcher would also like the treatment of methodological considerations, demographic and sociocultural correlates of psychopathology, and the causes and precipitants of psychiatric disorders and maladjustment.

If one approaches the book from the clinical vantage point, however, one finds that the different types of psychiatric disorders and adjustment problems practically replicate all *DSM-III-R* main categories. From the sociological point of view, the section that clarifies concepts such as culture shock, ensocialization, acculturation, cultural competence, assimilation, pluralism, multiculturalism, anomie, and the characteristics of the receiving community is very useful indeed. The public health official may refer to chapter six on the different strategies used by public health agencies, government bodies, volunteer organizations, churches, and colleges and universities to deal with the problems of migrants. This seems to be, in fact, the best part of the book, particularly its selections on primary and secondary prevention, phasing of public health efforts, and the development of a treatment system. The last section has to do with special aspects such as the study of refugee children, families, and adolescents and the need to establish "culturally sensitive psychiatric care." Special patient subgroups, such as unaccompanied minors, interracial children, alienated refugee adolescents, and married minors, as well as different sources of collective care, are paid due and competent attention.

As the reader oscillates among these different perspectives, he or she may wonder about the real nature and focus of this book. Sometimes it reads like a clinical text, other times like a research manual, occasionally like a socioepidemiologic review, and still other times like a purely descriptive, cookbook type of publication. As trite as it sounds, perhaps the book's strengths are also its main weaknesses. The broad scope of occupations and professions (from legislators to bureaucrats, from health planners to the clergy, from relief workers to social scientists) to which the book is addressed perhaps does a disservice to the thoroughness and solidity that one could expect from a truly scholarly work by a well-known expert. There are excellent conceptual and clinical descriptions, methodological innovations, instrumental selections, and bibliographical sources. Unfortunately, there are also sweeping generalizations and needless repetitions of notions such as intergenerational conflicts, incidence and prevalence, expectations, and biased migration. There is precious little material on ethnopsychopharmacology and almost none based on statistics and epidemiologic findings. One would have wished to see more comparative tables and as much hard data as possible to counteract charges of "softness" in the research conducted in this and other sociopsychiatric areas. In fact, with all its advocacy for research and the good suggestions that the book makes, one is left with the impression that not much has necessarily been done. At times it seems clear that the quick pace of the book reveals it to be a prelude to a more solid work, the result of reflection, objectivity, and in-depth analysis of the existing data. This is certainly a justifiable hope.

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Psychiatric Care of Migrants: A Clinical Guide, *by Joseph Westermeyer, M.D., M.P.H., Ph.D. Washington, D.C., American Psychiatric Press, 1989, 230 pp., $21.95.*

As noted by Dr. Judith Gold in the introduction to the Clinical Practice Series of the American Psychiatric Press, the series is designed to "provide readers with books that give the mental health clinician a practical clinical approach to a variety of psychiatric problems. These books will provide up-to-date literature reviews and emphasize the most recent treatment methods" (p. ix). *Psychiatric Care of Migrants,* the tenth book in the series, meets all these objectives and is a resounding success.

The book's scope is quite broad, since migrants are defined as "those who change their place of residence for any purpose or for any period of time. Included are . . . students going away to school, transferred or migratory workers, people whose work may necessitate travel, tourists, visitors, wanderers, refugees, and those returning home after a migration" (p. 11). The mental health of migrants is affected by a great number of variables, such as the migrant's personality, mental and physical health status, ethnicity, and life stage; the voluntariness and duration of relocation; the degree of similarity between the culture of origin and that of resettlement; presence and extent of victimization; and government determinations such as legal rights and access to social programs. Each of the listed variables easily could take up a book; ethnicity alone is a topic so vast that entire libraries are devoted to it.

Joseph Westermeyer is among the most prolific and respected cultural psychiatrists in the world. His extensive clinical experience with different migrant populations is evident throughout the volume, which is divided into chapters on theory, psychopathology, clinical assessment and management, and therapies (somatic, psychological, and social). The book does not get bogged down with minutiae but, rather, presents a structure for understanding the psychiatric problems of migrants. It also provides an approach to the collection of appropriate data from this class of patients so that the data can be analyzed into a meaningful diagnostic formulation and so that remedies, including medications, ECT, individual and family therapy, reconstruction of social networks, and advice that a patient return home, can be used properly.

Particularly impressive are the book's liveliness, skillful use of references, and clinical advice on a variety of topics, such as early postmigration substance abuse, false-positive Mini-Mental State Examination scores in poorly educated or elderly patients, the tendency of some translators to "normalize" a patient's psychopathology, identity problems of cross-racially adopted children, the effect of folk remedies on compliance with pharmacotherapy, and the specialized use of confrontation.

In sum, this is an unpretentious, easy-to-read, unique book that presents a great deal of general information in a straightforward manner. It fills a definite void in the psychiatric literature, and I heartily recommend it to all clinicians who work with migrant populations.

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Hispanics and Mental Health: A Framework for Research, *by Lloyd H. Rogler, Robert G. Malgady, and Orlando Rodriguez. Malabar, Fla., Robert E. Krieger, 1989, 154 pp., $19.50.*

This book is one of a long series of monographs from Fordham University's Hispanic Research Center. The material is presented in a conceptual framework that gives a broad overview of mental health research in Hispanic issues. It is basically an introductory work on the psychosocial aspects of mental health among Hispanic groups and is not intended to be comprehensive.

The authors begin with a discussion of research problems at the micro level, dealing with factors proximate to the lives of individuals. The approach is multifactorial and examines cogent issues in research on Hispanic groups. For example, it discusses discrepancies and problems regarding psychometric testing in minority populations and brings up differential normative performance as an issue in psychological testing. The need for more work in multidimensional personality tests to prevent bias when examining across populations is well discussed. The overall examination of test bias is very useful, and the monograph discusses controversial areas without enmeshing the reader in superfluous material.

The discussion on cultural, ethnic, and language barriers in psychiatric diagnostic settings is balanced and comprehensive. This discussion is also done with sensitivity without losing systematic objectivity. The authors clearly demonstrate the complex dynamics that operate when the primary language of the examiner is different from that of the patient.

Chapter six addresses the effect of deinstitutionalization on mental health issues among Hispanic groups. The effect of hospitalization and deinstitutionalization on family relationships is well presented. The authors demonstrate important issues in the role of family dynamics, unemployment and social status as critical factors in comorbidity, and other factors that would affect mental health issues in minorities.

Chapter seven stresses the need for an expanded multidisciplinary vision of mental health research. We fully agree with this view. Furthermore, it would seem that concurrent inclusion of psychosocial, cultural, and biological variables should be topics of inquiry.

There are several good points about this book. The material is presented in such a way as to be generalizable to all ethnic groups. The authors recognize the need for multidisciplinary research teams. The book serves as a good overview for the beginner in the field of research on Hispanic groups. Clinical vignettes for each phase of research are given to underscore points being made about cultural sensitivity. The book clearly points out factors that need strong consideration in any psychosocial research focused on Hispanic populations, including the impact of acculturation and social economic status. The authors also point out problems faced in mental health research among Hispanic groups caused by our limited knowledge about epidemiology in this area and by sampling problems in these heterogeneous populations.

The book does have some minor drawbacks. It has a tendency to focus more on Puerto Ricans than any other Hispanic subgroup. The enormously heterogeneous nature of Hispanic peoples is not reviewed thoroughly and lucidly enough perhaps, which skirts one of the most difficult research problems in this population. The subject index is rather sketchy, and much of chapter seven is redundant. One of the major problems with the book is that it does not address biological issues such as brain disease and organic psychiatric disorders, although this area is very underaddressed in research on Hispanic groups. Issues concerning substance abuse are also not presented as well as they could be.

With all things considered, however, we feel that this is a very valuable book. It is an up-to-date and accurate overview of the state of the art in mental health research among Hispanic groups. It clearly shows why more work needs to be done. As this diverse segment of the population continues to grow, mental health research will be increasingly important in the next decade. With so much more work required, we hope that this book will stimulate young and experienced researchers alike to do more work in this area. The authors provide facts that could serve as a basis for designing mental health research studies among Hispanic groups. The book could also provide a framework to achieve a goal the authors clearly define as crucial—the provision and funding of long-term longitudinal projects.

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ART

Art and Psyche: A Study in Psychoanalysis and Aesthetics *(1985), by Ellen Handler Spitz. New Haven, Conn., Yale University Press, 1989, 188 pp., $11.95 (paper).*

Scientists have long been aware of the beauty of great science and puzzled about both its origins (i.e., where does science come from?) and its aesthetics (what makes it beautiful?). We have also become interested in the science of great art, in its origins, the process of creativity, and our own aesthetic response. Although other psychologies have studied these issues (e.g., Sloboda's cognitive psychology of music), the major themes, starting with Freud's own contributions, have been psychoanalytic. Spitz's book is an "attempt to catalog or structure this dialogue between aesthetics and psychoanalysis" (p. 1). As her work illustrates, she is uniquely qualified for the task. She is a scholar trained in both aesthetics and psychoanalysis and able to translate jargon and theory, both theirs and ours, into comprehensible English with understandable referents.

Spitz examines psychoanalytic approaches to why and how we make art, to the artistic product itself, and to our response to it. She traces the history of psychoanalytic theory in our understanding of these: art as sublimated erotic and/or aggressive wishes as modified by defense; as originating in the autonomous ego and related to play; as an offshoot of development and object relationships, as separation-individuation; and as transitional object.

Most psychoanalytic contributions to the study of art have focused on pathography—the relationship of the artist's inner life to the artistic product. Spitz refers to Freud's own work in the area as "fictive"—imaginative interpretation. However, an attempt to understand the artist's psychic reality and the meaning of events often requires more attention to the historical context of both the artist's life and his or her art. Spitz offers Liebert's work on Michelangelo as an example of this "documentary" approach to pathography. A third approach to pathography Spitz calls "thematic," as seen in Wolfenstein's studies of the role of loss in Magritte's oeuvre, in the thread of "multiple representations and transformations . . . of his mother's death" (p. 76).

Psychoanalysts have also attempted to interpret the texts and objects themselves, independent of the producer, as autonomous, the equivalent of a "new criticism" in response to the Romanticism of pathography. Ego psychology has also tried to examine the relationship of style to character, the role of temperamental givens. Spitz, drawing on the work of Mahler, Winnicott, and Stern, explores developmental issues such as the role of fusion, illusion, and magical omnipotence in both the making of and response to art.

The book structures the dialogues in various ways: id, ego, or developmental and object relations approaches; "the nature of the creative work and experience of the artist, the interpretation of works of art, and the nature and givens of aesthetic experience" (p. 167); and "definition of text, a critical mode, and a particular set of aesthetic problems" (p. 171). Through the accuracy of her scholarship, her breadth of knowledge, and her clarity of thought, Spitz provides us with a reasonable framework, a prolegomena, within which to advance our understanding of the making, the meaning, and the message of art.

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The Discovery of the Art of the Insane, *by John M. MacGregor. Princeton, N.J., Princeton University Press, 1989, 377 pp., $49.50.*

The author posits that the insane are capable of producing pictorial art. He also finds it an interesting phenomenon of psychiatry, art criticism, and aesthetics that it remained so long undiscovered and that, once discovered, it has been so long unappreciated. Dr. MacGregor, an art historian and psychoanalyst, provides a brilliant survey of the artists who discovered the art of the insane, such as Hogarth, Dubuffet, Dali (who professed himself mad), and Klee; artists who were hospitalized for insanity; patients who became brilliantly artistic during their psychoses; psychiatrists who took an interest in the art of the insane as an interesting symptomatic behavior; and, finally, those who appreciated the art itself. The chapters are immensely rich in scholarship, illustrations, and insight. This, together with the author's lucid writing style, makes for an interesting, informative, and pleasurable read.

Larger questions, such as the changing views of insanity, the relationship between creativity and insanity, the "insanity" of modern art (a criticism their contemporaries leveled at the expressionist painters), and the function of art, all receive excellent attention. MacGregor's background in art history is evident in the ease and brilliance with which he provides the necessary historical-cultural background for each artist. He is able to dissect what is unique to each artist and distinguish it from the contemporary aesthetic standards of the time so that the focus of the unique psychotic contribution to the artwork can be considered.

MacGregor's psychoanalytic perspective lends depth to his work, but it leads him to an unnecessarily pessimistic conclusion. He argues that the art of the insane remained undiscovered because it was too threatening to appreciate that the insane might possess artistic insight as part of their psychosis. Psychiatrists, who might have been expected to appreciate the work of the insane, are no different from the rest of the nonpsychotic world in this regard and in fact may act in collusion with the societal "need" to disavow any meaning to the creative efforts of the psychotic. MacGregor argues that the need to silence these potentially frightening images of our deepest selves may become inextricably intertwined with the wish to treat. He quotes the surrealistic artist Artaud's view of psychiatry as an "inborn enemy of all genius" (p. 285). One suspects that this is an opinion that MacGregor views sympathetically in some instances.

Does treatment of insane artists destroy their creativity? In particular, do chemical treatments provide creative straightjackets? MacGregor places a high value on providing psychotic patients with an opportunity to communicate their experiences—especially if they happen to have artistic talent—and fears that short hospitalizations and chemical treatments do not permit this. There is much to this view, but most readers will find it overstated.

MacGregor's theory of artistic production in the insane is that the insane artist attempts to regain contact with a lost or very disturbed reality by the production of art. This was Freud's theory of psychotic symptom formation, and its application to artistic work is questionable. One is always left with the problem of talent. Everyone is capable of doodling and smearing paints, but only a few produce art. It remains unclear whether any special relationship exists between insanity and creativity. Finally, one could argue that artists do not simply seek to construct a substitute reality that will connect them to a saner reality but may seek to repair the damage they themselves have done to reality or even to express gratitude to those who try to maintain contact with them even as their capacity to respond fails. I know of an alcoholic street person with schizoaffective disorder who is periodically admitted to our hospital with violent behavior motivated by rescue delusions. As he recovers he regularly begins to produce drawings and paintings of considerable merit. He then gives these as gifts to the nurses and mental health workers. The hospital staff has begun to see the beginning of his artistic production as a sign that the patient is adequately medicated and feeling better.

MacGregor never professes to resolve the problem of insanity and art. The roots of creativity in any individual, insane or otherwise, remain an enigma. The book does, however, alert us to the fact that the insane, like any other group that becomes isolated and alienated from the main body of society, have something to say, and that it behooves us to attend.

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THERAPIES

Cognitive Therapy With Schizophrenic Patients, *by Carlo Perris, M.D. New York, Guilford Press, 1989, 240 pp., $27.50.*

At last, a breath of fresh Arctic air wafts over psychiatry's most persistent conundrum—schizophrenia. While American psychiatry preoccupies itself with how many Schneiderian symptoms can dance on the head of a putatively schizophrenic person or which receptors and neurotransmitters are affected by the newest psychotoxin, at least one Scandinavian writer is interested in an innovative psychosocial application of cognitive therapy to treat madness. Dr. Perris is an Italian emigré in Sweden whose previous work has been primarily in biological research on depression.

It is surprising that an approach through cognitive therapy to schizophrenia has not been in wide use already because, for one thing, thought disorder is a classical, well-agreed-on characteristic of schizophrenia and, second, thanks to the work of Beck et al. (1) and others, cognitive therapy is certainly fashionable now—especially for treating depression.

There is probably more replicated, consistent, and persuasive research evidence about the various types of deviant communication (including both attention and language use) specific to patients with schizophrenia and their families than any other set of closely related variables. In 1975, after a comprehensive review of the family studies then available, Jacob (2) concluded that they indicated that disorders of thinking (in contrast to variables related to roles and affect) were specific to families with a schizophrenic offspring. More recently, Shenton et al. (3) have provided additional supportive data. Thus, Perris's approach addresses what may be the heart of the matter for many, if not all, persons labeled "schizophrenic."

Although this is a short book, it is dense. In the 70 pages that make up the introductory chapters of section one, Perris covers subjects usually receiving book-length treatment, such as schizophrenia, diagnosis, outcome, vulnerability, cognitive development, and a number of others. Experts in each area may find the reviews in this heavily referenced tour de force oversimplified or incomplete. However, they indicate that the author has done his homework.

For me, Perris's major contribution appears in the two chapters that make up section two. Schizophrenia is not likely to be amenable to improvement from a few weekly hours of compartmentalized psychosocial care. One reason why intensive psychoanalytic psychotherapy in a hospital setting has not proven to be a powerful treatment is that the hospital context with which the patients interact for 163 or 164 out of 168 hours in a week is usually neither defined nor tailored to enhance the effects of the psychotherapy. One hour of the most intensive, thoughtful, insightful, even charismatic psychotherapy can disappear into the next 23 hours of ward events. By providing a 24-hour-a-day integrated treatment package, Perris avoids this frequently fatal conceptual pitfall of psychosocial therapy. To conduct his cognitive therapy program, Perris started two small (6–8 patients), homelike, intensive, holistic "centers" focused on providing an atmosphere like that in a family group in a normalizing community environment. His centers are well staffed, principally by nurses trained in cognitive therapy. To promote the sense of normality further, the program is based on the academic calendar, and each "student" is asked to sign up for a full year's work. In the summer, the "students" go away on vacation—as is usual in Sweden for people of every social status. The centers admit any patient with post-acute *DSM-III-R* schizophrenia who has "not been entirely burned out by prolonged hospitalization" (p. 81). The use of medication is minimal; however, patients learn to be responsible for their own medicines.

These two chapters also describe in detail the principles and practices of the overall milieu context for the individual cognitive therapy program that is the subject of the book's final section. It is clear that the milieu program has been modeled after the well-researched Soteria-Crossing Place programs (4, 5). Because of a reliable payment mechanism (national health insurance), Swedish therapeutic programs need not be located in hospitals. Unfortunately, such innovative programs do not usually qualify for third-party reimbursement in the United State (6).

Holistic treatment packages that rely on cognitive therapy in normal milieux are exciting in concept and execution. I am certain they will work—however "work" is defined. My major criticism is that a very research-oriented psychiatrist missed an opportunity to investigate exactly how powerful an effect such a program has and to compare one theoretical model with another. We badly need a study of the cognitive therapy milieu approach of one Perris house with the interpersonal-phenomenologic approach of a Soteria-type house for groups of randomly assigned patients followed for 5 or more years.

Still, *Cognitive Therapy With Schizophrenic Patients* presents a fresh approach described in enough detail to allow replication. Will anyone take up the challenge?

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Social Skills Training for Psychiatric Patients, *by Robert Paul Liberman, William J. DeRisi, and Kim T. Mueser. New York, Pergamon Press, 1989, 246 pp., $24.50; $14.95 (paper).*

It is refreshing indeed to find that some academic psychiatrists remain seriously interested in the problems of psychosocial adaptation experienced by most of the long-term veterans of the mental health nonsystem. Liberman and his colleagues have devoted many years to developing, researching, implementing, and providing packaged modules for social skills training to be used with the most problematic users of mental health services.

This five-chapter, seven-appendix "how to" volume provides a helpful, practical orientation to a field not usually in the purview of psychiatrists. It also contains a useful but not entirely inclusive (more on this later) annotated bibliography. The kinds of training described in this volume are usually given in rehabilitation settings—places that have only tenuous, if any, links to psychiatry. Nevertheless, I believe it important that psychiatrists have at least a working knowledge of these types of effective psychosocial interventions. I am afraid, however, that this scholarly volume will not receive the readership it deserves within our profession because it is, to put it bluntly, pedantic and rather boring. Unfortunately, this is a reasonably accurate reflection of the nature of this particular beast. It is, after all, a technology. Like computer program manuals, it is difficult to make scintillating. However, these programs are for real people, not machines. Somehow, the personhoods of the subjects of the illustrative cases are so muted as to be lost. It must be admitted, however, that the book is in keeping with academic psychiatry's current technological, biomedical *Zeitgeist.* In a sense, this volume may be seen as a translation of a psychosocial intervention art form into a more acceptable and replicable laboratory-test-like recipe.

For me, a major problem with the book is its failure to attend properly to the critical importance of the relationship of the social skills trainer with the trainee. Discussion of the need for a therapeutic alliance is relegated to the last chapter, "Overcoming Resistance to Social Skills Training," which reads as if it were included mostly for the sake of completeness. There is excellent consensus in the psychosocial intervention research literature that little behavioral change can be expected without a good working therapeutic alliance. More attention to this area might also have made this volume more human and readable.

About the bibliography, there are two glaring omissions: Paul and Lentz's seminal study of remarkably effective, behaviorally focused inpatient milieux for extremely long-term backward patients (1) and Lukoff et al.'s comparison of a "holistic health" inpatient milieu with a behavioral one for long-stay patients (2). The holistic approach was as successful as or perhaps more successful than the behavioral one. What is especially perplexing about the latter omission is that this study was conducted in Liberman's own Camarillo State Hospital setting, and he is one of the authors.

Despite these shortcomings, the authors have done the field a great service in providing a very compact, useful description of how to conduct a known effective psychosocial intervention program.

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Cognitive Therapy for Depression and Anxiety: A Practitioner's Guide, *by Ivy-Marie Blackburn and Kate Davidson. Chicago, Mosby-Year Book, 1990, 221 pp., $39.95.*

The authors are cognitive therapists who have drawn on their clinical experience to describe many of the practical issues of the management of depressed and anxious patients. In particular, Blackburn has made a number of contributions to the clinical and research literature on the cognitive model and the treatment of depression. Most recently, she published a self-help book for depressed patients based on cognitive therapy principles (1).

The present volume is divided into two parts. The first addresses basic issues such as the description of the syndromes of depression and anxiety, the cognitive therapy model, the skills required for successful cognitive therapy, and specific cognitive therapy techniques for depression and anxiety. The second part provides case transcripts of a patient with major depression and a patient with generalized anxiety disorder. These two cases are followed from the initial interview and case conceptualization to the termination of therapy. The authors conclude with a discussion of the problems commonly encountered in cognitive therapy and their resolution.

One of the very positive features of this volume is that Blackburn and Davidson consider both depression and anxiety. The basic rationale and most of the techniques for treating these disorders are identical, and it becomes clear in the case descriptions that there is a great deal of transfer from the treatment of depression to the treatment of anxiety. These case transcripts and the authors' commentary make concrete many of the elements of cognitive therapy that would not be apparent from simply reading descriptions of the techniques. Moreover, these transcripts give the reader some sense of how different cognitive interventions fit together over the course of treatment with a patient.

There were other positive features of this volume as well. The authors are British; however, there is little use of British idiom that might interfere with the American reader's understanding of the material. The volume is clearly written and well organized. In the early chapters, devoted to the underpinnings of cognitive therapy, key concepts are emboldened and placed in the margin. This allows the reader to quickly scan for relevant concepts. Overall, the book should serve as a good introduction to cognitive therapy for the novice and experienced clinician alike.

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Brief Therapy Approaches to Treating Anxiety and Depression, *edited by Michael D. Yapko. New York, Brunner/Mazel, 1989, 384 pp., $39.95.*

Before discussing the specific aspects of this book, I should like to discuss the general area it is involved with—strategic psychotherapy. As psychiatry has become more interested in quantifiable, reproducible results, those areas which are easier to quantify (e.g., epidemiology and psychopharmacy) have tended to come to the fore, while those which are difficult to quantify (e.g., interpersonal interactions) tend to be relegated to "clinical art" until such time as we achieve greater sophistication and make the effort to quantify them. (Of course, there have been some recent strides in quantifying the area of short-term psychotherapy of depression.) Strategic psychotherapy is therapy evolved from the teachings of Milton Ericksen on hypnotic techniques. Although it appears that some of the authors in this volume have some interest in the question of classification of treatment and response, until recently most of these practitioners believed that each case was unique and should not or could not be combined into treatment categories. This left psychiatric practitioners confused as to whether and how they could integrate these teachings into their practices, which are syndrome and classification oriented. To demonstrate the potential value of paying attention to interpersonal response sets, I will give an example from a recent personal experience.

I staff a psychopharmacology maintenance clinic one day a week at the Veterans Administration. Two types of time slots are available: 20 minutes for routine stable patients and 30 minutes for patients who appear to be having some difficulty. On occasion, due to scheduling processes, a routine visit will be scheduled in a 30-minute slot. Mr A, a stable patient with the diagnosis of schizoaffective disorder, appeared at my 30-minute time slot. I had seen Mr. A only three times, although he had been an outpatient clinic patient for 38 years and had seen other physicians. Although not uncooperative, Mr A was emotionally attached to his medication regimen and was resistant to questions or suggestions that might lead to a change in it. On this occasion he said that he was feeling fine and wanted a renewal of his medication. Fearing he was not revealing some difficulties that had caused him to be referred to the 30-minute visit, I reminded him that the 30-minute time slots were used only for "people in difficulty or with special problems." After thinking a moment, he gave a detailed history of 40 years of severe obsessive-compulsive symptoms that he had never revealed to previous caregivers. Asked why he waited so long to mention this, he replied, a bit sheepishly, "It was kind of personal." This is an example of where an inadvertent change in response set resulted in substantial changes in treatment. (Due to his resistance to medication changes Mr. A was referred for behavioral therapy for his obsessive symptoms.)

This book is a compilation of papers presented at the Fourth Annual Conference on Hypnotic and Strategic Interventions held at the Milton Ericksen Institute in San Diego in 1988. The writing style is consistently readable throughout, and the book is well edited and has a wealth of clinical examples. There are four sections. The first is the keynote address by Martin Seligman. Seligman talks about personality characteristics (he calls them attributional styles) that make people either vulnerable or resistant to emotional illness and stress. He cites relevant clinical examples from psychology that appear to dovetail with the extremely small literature to be found in psychiatry. I felt this was a chapter well worth reading.

The second section is entitled Interventions for Depression and consists of eight chapters. Two of these deserve individual mention. One is a theoretical piece by Rossi, which is a little slow going. The second is a discussion by Yapko of patients' relationships to time in regard to the hypnotic treatment of depression, which should be cited for its organization. The remaining chapters are clinically oriented descriptions of how different practitioners have used hypnotic techniques in different clinical situations to treat depression. Although the diagnostic categories in the chapter by Salemeh are a bit idiosyncratic, the chapters are generally interesting and valuable.

The third section is entitled Interventions for Anxiety. This section discusses in a relatively detailed way various strategies by which hypnotic techniques can be used to help alleviate anxiety symptoms. Several approaches are discussed, and readers might well find one that suits their therapeutic study.

The fourth section, Therapeutic Approaches for Anxiety and Depression, consists of several chapters on treatment techniques that apparently the editor felt were not easily categorized into the previous sections. Except for the chapter on treatment of anxiety and depression in chronic pain, which is probably of interest to specific practitioners, the subject matter of these chapters resembles that of sections two and three.

In sum, this is a readable, well-written book on hypnotic treatments for anxiety and depression. Since the level of development of this area is closer to clinical art than clinical science, it will probably be of more interest to clinicians than to researchers. For clinicians it certainly is worthwhile to gain some idea of what techniques might be available in this area.

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A Concise Guide to Group Psychotherapy, *edited by Sophia Vinogradov, M.D., and Irvin D. Yalom, M.D. Washington, D.C., American Psychiatric Press, 1989, 169 pp., $18.50 (paper).*

Despite its proven power, efficacy, and cost effectiveness as a treatment modality, group therapy has been eclipsed by other types of treatment since its peak in the 1970s. Why this is the case is uncertain and subject to speculation. In part, the decline of group psychotherapy may be due to the waning of the encounter movement of the 1960s and 1970s, a great boon for group psychotherapy. Nevertheless, group therapy remains a powerful and stimulating tool for both treatment and training.

The appearance of this compact and accessible guide to group therapy follows a trend in the "manualization" of treatment (1–3). This small volume neatly distills Yalom's classical thinking about the functioning of therapy groups. Covered here are topics ranging from basic concepts to the rationale for group therapy, curative factors, and practical matters like creating a group, tasks and techniques of group leaders, managing problem patients, exercises to structure and catalyze group process, writing process notes, and applications of groups to special settings and clinical problems.

The focus here is straightforward, easily digestible, and entirely lacking in jargon or ideological ax grinding. The book is detailed enough to be useful, yet accessible enough to be a handbook. The book is well indexed and the layout allows for tireless consultation.

A Concise Guide to Group Psychotherapy will be useful for trainees in psychiatry, psychology, and social work as they do group therapy. Supervisors will find the book extremely useful in educating trainees in basic group therapy issues. Although the book is not a substitute for careful supervision, it is a practical adjunct to the supervisory process.

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Reprints of Book Forum reviews are not available.

Letters to the Editor

The *Osheroff* Debate: Finale

SIR: A number of issues have been raised by Dr. Stone's response and by others who have written letters to the Editor about the *Osheroff v. Chestnut Lodge* discussion (1, 2). I will address 1) clinical issues regarding the diagnosis and treatment of Dr. Osheroff, particularly the diagnosis of personality disorder (3), and 2) my assessment of the implications of this case for psychoanalysis and the psychodynamic school of American psychiatry.

Dr. Stone and other apologists for Chestnut Lodge make much of Dr. Osheroff's having a diagnosis of narcissistic personality disorder. This is somewhat surprising, since the personality issue was not salient on admission or in the early weeks of hospitalization. According to hospital records, the discussion at the case conference held about 6 weeks after Dr. Osheroff's admission emphasized the necessity of long-term intensive psychotherapy for his psychotic depression. In subsequent clinical discussions, at the time of his transfer to Silver Hill, and as the legal proceedings developed, the diagnosis of Dr. Osheroff's personality disorder became increasingly prominent.

Dr. Osheroff has reviewed the evidence for this diagnosis in a letter to the Editor, and I have little to add. I do, however, wish to comment on the function of the personality disorder diagnosis. There are two purposes served by labeling/diagnosing Dr. Osheroff as having a narcissistic personality disorder. First, the diagnosis legitimizes post hoc the decision of the clinical staff at Chestnut Lodge to persist in psychotherapy without use of biological treatments. Almost all psychiatric experts, including Dr. Stone, and the APA *Manual of Psychiatric Peer Review* are explicit in their statements that, for psychotic depression, biological treatments are necessary and psychotherapy plays a secondary role. How, then, to justify the decision of the Chestnut Lodge staff not to give medication to Dr. Osheroff? By shifting the focus of the clinical diagnosis from his depression to a presumed personality disorder. Second, diagnosing/labeling him as having a personality disorder serves to make his complaints less credible and to invalidate his efforts to address his grievances and seek justice in the legal system. What an irony that a professor at Harvard Law School should use psychoanalytic characterology as a means to deny justice to a patient who has been treated poorly and who suffered damages in his personal life, family relations, professional income, and hospital staff status.

Even if the personality disorder diagnosis were accurate, it should not have influenced the use of biological treatments for a psychotic depression. Almost all experts, including Dr. Otto Kernberg, a leading psychoanalyst, agree that with the emergence of a psychotic depression, treatment of the depression takes precedence over treatment of the personality disorder.

The psychodynamic school has become increasingly preoccupied with characterology, having almost completely abandoned the symptom neuroses. Considerable impetus for this shift was given by the promulgation of *DSM-III* and the delineation of axis II for personality disorders. The validity of most of the personality disorders delineated in *DSM-III*, including narcissistic personality disorder, remains unestablished. More important for this case is the tendency in clinical discussions and theoretical discourse to use the term "personality disorder" in a pejorative fashion as a moral judgment. To label an individual as having a personality disorder is to render him or her less entitled to administrative and legal protection and less powerful politically.

Related to the focus on characterology is the tendency of the psychodynamic school to avoid issues of evidence for therapeutic efficacy. In trying to explain Dr. Osheroff's recovery from depression after his transfer from Chestnut Lodge to Silver Hill, Dr. Stone invokes the fanciful explanation that the transfer involved a fantasied triumph of Dr. Osheroff's narcissism over the doctors and institutions. We are not given any evidence for this interpretation. If Dr. Stone and the staff of Chestnut Lodge had believed in the effectiveness of this intervention, they could have transferred Dr. Osheroff at many points during his 7 months of hospitalization at Chestnut Lodge. There is no reported study of this intervention as a treatment for psychotic depression. In contrast, there are numerous randomized, controlled trials of the efficacy of ECT and the combination of tricyclic and neuroleptic medications in the treatment of psychotic depression. What strange clinical logic to ignore available evidence in favor of a conjecture based on doctrine.

Dr. Stone casts his discussion as a debate between psychodynamic psychiatry and scientific psychiatry, equating scientific psychiatry with biological psychiatry Here, again, there is an irony: why doesn't psychodynamic psychiatry attempt to be scientific? Why does psychodynamic psychiatry not abide by the usual scientific principles regarding falsifiability, experimentation, replication, and concern for reliability and validity (4)?

The psychodynamic school was the dominant school in clinical, research, and academic settings in American psychiatry in the period after World War II. The senior leadership in the Public Health Service of the federal government was very sympathetic to psychoanalytic ideas and methods in the early decades of the National Institute of Mental Health (NIMH) program; the psychoanalysis of many psychiatric researchers was subsidized by federal money as part of a career development program. The chairpersons of leading departments of psychiatry in medical schools were often psychoanalysts, and the "best and brightest" of psychiatric residents through the 1950s and 1960s sought psychoanalytic training.

That is now changed. Psychoanalysis is now on the defensive intellectually and scientifically. New schools of psychiatry—biological, social, behavioral—have emerged, and new forms of psychopharmacologic treatment and psychotherapy have come forth to challenge the therapeutic monopoly of psychoanalytic ideas. The leadership at the Alcohol, Drug Abuse, and Mental Health Administration and NIMH is increasingly biological in orientation, and search committees for chairpersons of departments of psychiatry are interested in neuroscientists and, at times, have a negative attitude toward psychoanalysts.

How has the psychodynamic school responded to these changes? Unfortunately, by apology and argument ad hominem. It has not generated evidence for its claims of therapeutic efficacy. In this respect it is interesting that proponents of the newer psychiatric schools have increasingly used randomized, controlled trials to support claims for the efficacy of psychopharmacologic and behavioral therapies and as weapons in the rivalry among schools of psychiatry and, particularly, the interprofessional rivalry between psychologists and psychiatrists.

The title of Dr. Stone's paper (2) is indicative of this response of the psychodynamic school. The title announces his reply to my *indictment* of psychoanalysis. This is unfair to me. "Indictment" has a specific meaning in criminal law, implying a violation of criminal statute. While I am critical of psychoanalysis and skeptical of some of its claims, to invoke the term "indictment" is to go far beyond my argument. It is not an accurate representation of my views, and it serves to mobilize the believers in psychodynamic therapy by discrediting me and attributing to me a position that I have not taken.

Dr. Stone's argument seems to be that the professional and scientific difficulties that the psychodynamic school is experiencing result from the use of the courts by scientific/biological psychiatrists like myself to advocate our professional views. Of course, I have a point of view and have expressed it in various settings, including court cases such as the *Osheroff* case. Dr. Stone and his colleagues do not hesitate to express their point of view. There is nothing conspiratorial, undemocratic, or unprofessional in this advocacy. In fact, it was Dr. Stone who first drew attention to this case in the *New England Journal of Medicine* (5).

The current problems of psychoanalysis and the psychodynamic school are not the result of critics such as myself. Would that we were so powerful! Rather, the psychodynamic school has failed to respond adequately to new developments. For example, consider the status of the symptom neuroses: phobias, obsessions, compulsions, anxiety, depression, and dissociative states. In the past, psychoanalysis has contributed greatly to our diagnostic and therapeutic understanding. The situation has changed dramatically. If one looks at the programs of recent APA annual meetings, one finds that in the many lectures, discussions, and symposia on obsessive-compulsive disorder, phobia, depression, and panic disorder, the psychoanalytic school was hardly represented. What new contributions have psychoanalysts made to the understanding and treatment of phobias? Is there any evidence about new psychoanalytic treatment of obsessive-compulsive states?

Moreover, the new treatments—psychopharmacologic and behavioral—have supported their claims for efficacy by randomized, controlled trials. There are no reports on controlled trials of dynamic treatment of these clinical states. A few efforts are now underway, namely, the work of M. Horowitz on stress disorders, of L. Luborsky and his associates on the use of supportive-expressive therapy for heroin addicts maintained on methadone and, more recently, for patients with depression, and the efforts of a psychoanalytic study group on panic led by A. Cooper and K. Shear. However, these efforts are at a relatively early stage in their development and have not had an impact on research thinking or clinical practice.

Let me make my position on psychoanalysis and psychotherapy explicit. I am not a biological psychiatrist, nor am I hostile toward psychotherapy. I do not rely exclusively on psychopharmacologic agents, and I have been active in psychotherapy research for 20 years. I am not hostile toward psychoanalysis. My dominant feelings about psychoanalysis are frustration and disappointment.

There is resistance within the psychoanalytic community to confronting the issues of the scientific status of psychoanalysis and the need to generate evidence for the claims of efficacy of psychoanalysis and psychodynamic psychotherapy. Unless these issues are grappled with by the psychoanalytic leadership, I am pessimistic about the future of our profession, which has been greatly enriched by psychoanalytic ideas and psychodynamically oriented teachers and clinicians.

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Dr. Stone Replies

SIR: This coda to the *Osheroff* dispute seems to be in the adversarial mode Dr. Klerman espoused when he chose to testify against Chestnut Lodge. Here Dr. Klerman labels me an "apologist" and implies that I have questionable motives.

Some of his comments might suggest to readers that, like Dr. Klerman, I had direct personal or professional involvement in this matter. I must therefore reemphasize the fact that I was not retained as an expert witness, nor did I have any clinical connection with Chestnut Lodge. My only involvement has been my academic commentaries on the legal significance of the litigation. In that connection, my response to Dr. Klerman's paper emphasized that he had mischaracterized the precedential value of a case settled out of court and that there was no legal authority for what he called the "right to effective treatment." Therefore, any standards based on his misunderstanding of the law were not valid. Furthermore, the standards he proposed had ominous implications for the psychodynamic school, and in the long run, his approach would be counterproductive even for the "scientific" psychiatry he favored. Dr. Klerman does not respond to these basic criticisms set out in my response. Instead, he replays two themes: the diagnosis and transfer of the patient and the scientific status of psychodynamic psychiatry.

As to the theme of the diagnosis and transfer, it should be recalled that Dr. Klerman asserted that a working diagnosis of narcissistic personality disorder was negligent, even though an affective disorder was also diagnosed. My response, based on published information, set out details of the clinical history omitted by Dr. Klerman which demonstrated that such a diagnosis was entirely plausible. I also emphasized the frequency of the narcissistic personality diagnosis in that time period as further evidence against Dr. Klerman's uncompromising judgment that his colleagues behaved negligently.

My suggestion that the diagnosis might have been reasonable at the time is apparently reprehensible to Dr. Klerman. He is prepared to borrow a familiar page from the antipsychiatry polemicists who refuse to recognize that a psychiatric diagnosis can be both clinically correct and personally offensive. Dr. Klerman, like many "expert witnesses," has simply overstated his case. To make his point, he is now willing to repudiate the *DSM-III* personality disorders. Ironically, in his original paper, adherence to *DSM-III* was the very standard of care he wanted to impose on his psychodynamic colleagues.

I continue to believe that the diagnosis of narcissistic personality disorder was not negligently made, nor was it intended to be pejorative or morally condemnatory. And I did not suggest that such a diagnosis would justify the 7-month course of exclusively psychoanalytic treatment at Chestnut Lodge. As Dr. Klerman recognizes, I clearly stated that when Dr. Osheroff's condition deteriorated and when there were obvious symptoms of a major depressive disorder, consultation and alternative treatment were indicated. Therefore, Dr. Klerman's statement that I "would deny justice to a patient" through psychoanalytic characterology is, at the least, ill considered.

Dr. Klerman finds my opinion about Dr. Osheroff's sudden and dramatic improvement after his transfer "fanciful" and illustrative of the "strange clinical logic" common to psychoanalytically oriented colleagues. He apparently prefers to believe that Dr. Osheroff's dramatic improvement was entirely due to the drugs he was given. Perhaps it will help readers to sort out this disagreement if I restate my understanding of the issues. First, before his hospitalization, Dr. Osheroff had several times been medicated for depression in exactly the efficacious fashion Dr. Klerman would require, without dramatic improvement. Second, Dr. Osheroff was at a therapeutic impasse at Chestnut Lodge, with an intense negative transference, when an experienced consultant suggested transfer to a different hospital. Third, Dr. Osheroff's own account of the effect of the transfer indicates that he experienced a profound psychological improvement before the time at which one would expect the medication to take effect. Also, the quality of his psychological improvement was unlike that usually seen in patients on a combined regimen of phenothiazines and tricyclics. Fourth, the psychiatrist who was directly responsible for Dr. Osheroff's overall treatment at the second hospital emphasized the importance of the different psychiatric milieu in the patient's dramatic improvement. Fifth, it has been my clinical experience that patients frequently benefit from a change when they are at a negative therapeutic impasse. The same (presumably efficacious) treatment works better when given by a different doctor in a different setting. If Dr. Klerman believes that this account demonstrates a "strange clinical logic" which he would eschew, then I am at a loss to know how he understands the role of transference in the clinical practice of psychiatry.

The second theme in Dr. Klerman's coda laments, as did his paper, the unscientific nature of psychoanalysis and its current decline. He adds only that the word "indictment" as used in the title of my paper discredits him. I must confess that my earlier word choices were harsher. It seemed to me that Dr. Klerman had done more than indict; he had, in fact, judged and sentenced. He had declared psychoanalysis and psychodynamic psychiatry obsolete by his scientific standards and had proposed legal barriers to their practice. Whether he did this out of frustration or hostility seems irrelevant. Certainly, his proposal would undermine the professional credibility of psychodynamic practitioners.

Dr. Klerman made two kinds of arguments against the psychodynamic school. First, he attacked the scientific status of psychoanalytic theory, citing the philosopher of science Grunbaum. Second, he criticized the lack of clinical efficacy studies, such as those required by the Food and Drug Administration for drugs. Neither of these arguments is new or original with Dr. Klerman. They have both been made by various critics for decades. What was novel was Dr. Klerman's insistence that they were now relevant to legal determinations of what constitutes negligence in the practice of psychiatry. Therefore, my response focused on the legal considerations.

Here I would briefly add that whether or not psychoanalysis is a "science" is a matter of competing definitions of science (1). Psychoanalysis is not a science as that concept is defined by logical positivists like Grunbaum or by the paradigm of biological materialism that now dominates much of American psychiatry. Biological materialism may eventually explain memory, but it will never explain memories. As long as psychiatry deals with human memories and the relation between symptoms and the human experience, it will need more than the limited understanding supplied by these narrowly defined concepts of science.

As to the efficacy arguments, Dr. Klerman's strict standard of scientific scrutiny has not been equally applied to the available clinical efficacy technology on which he relies. The recent disputes about the interpretation of the results of the NIMH collaborative research on treatment of depression (2) amply demonstrate the lack of scientific unanimity produced by current methods of studying clinical efficacy. One does not have to be a Luddite or an enemy of scientific psychiatry to suggest that until we know much more about the neurosciences, we are still crawling on our hands and knees. We are at the early stage of a long journey in search of definitively efficacious treatments for our patients.

Dr. Klerman, for the first time in this coda, explicitly acknowledges that he used the *Osheroff* litigation as an occasion to advocate his own professional views in court. He therefore confirms a basic thesis of my criticism. During the past two decades, psychiatry has been turning and twisting in the winds of litigation. At every turn and twist we were told, as Dr. Klerman tells us, that it was a matter of justice for patients. But in fact the impetus for legal change in this field has come from lawyers and self-interested professional experts who have advocated their own views. Sometimes the professionals, ignoring or discounting efficacy, were hostile to ECT or to antipsychotic medications. Typically, they sought to reject the medical model of mental illness and treatment. The one consistent result of this litigation has been to limit the discretionary judgment of the psychiatrist.

Dr. Klerman's attack is from the other side, so to speak, but it would have the same dispiriting result. It would narrow and limit our profession to a cookbook of recipes sent down from on high. The threat of malpractice liability invoked by Dr. Klerman and the fiscal discipline of managed care join forces in this cookbook mentality that now erodes professional autonomy in the name of science and efficacy. Our patients who need more than recipe treatments will be the victims.

I agree with Dr. Klerman that psychiatry "has been greatly enriched by psychoanalytic ideas and psychodynamically oriented teachers and clinicians." This enrichment took place even though the scientific criteria Dr. Klerman now mandates were never met. That may be a paradox for Dr. Klerman, but for me it demonstrates that the "learning" of psychiatry comes from a family of humanistic and scientific disciplines. Indeed, that is the vital attraction of the profession. The art of clinical practice is in weaving these disciplines together; science may be our guide but it is not our master.

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Thiazide Diuretics and Polydipsia in Schizophrenic Patients

SIR: The literature linking polydipsia, hyponatremia, water intoxication, and hyponatremic encephalopathy in chronic schizophrenic patients is voluminous (1). Several cases of polydipsia in which a thiazide diuretic is thought to have triggered water intoxication and its sequelae have also been reported (2, 3). We report here a serious case of hyponatremic encephalopathy that was very likely precipitated by hydrochlorothiazide and add the warning that polydipsia should be ruled out before thiazide diuretics are prescribed for patients with schizophrenia.

> Mr. A, a 32-year-old schizophrenic patient whose condition had been stable with a regimen of fluphenazine decanoate, 1 cc every 2 weeks, for more than a year, was hospitalized after his mother noted that he was more withdrawn than usual, not sleeping, and drinking excess fluids. The patient, hospitalized for 24 days, continued to receive fluphenazine decanoate injections and was also started on hydrochlorothiazide, 50 mg/day, for hypertension (his blood pressure was 150/90 mm Hg).
>
> Three weeks after discharge, Mr. A's mother found him in bed, diaphoretic and mute. He was admitted to the intensive care unit in status epilepticus, which was terminated with intravenous phenytoin sodium and diazepam. On admission, his serum sodium level was 108 meq/liter. A drug toxicity screen was negative. When he was given a short course of 3% normal saline while a large free water diuresis developed, his serum sodium level rose to 135 meq/liter in about 8 hours, suggesting that pituitary function was normal. He had no further seizures.
>
> Mr. A's mother reported that during the week before this hospitalization, he had been drinking 3–4 quarts of beer and up to 6 liters of soft drinks each day. He was also smoking 3–4 packs of cigarettes daily. Because of the large amount of liquid consumed, and because his serum sodium level was quickly corrected, a diagnosis of psychogenic polydipsia and diuretic-induced hyponatremia was made. The diuretic was discontinued, and the patient was discharged on a regimen of oral captopril, 25 mg t.i.d., to control hypertension. The suspicion that hydrochlorothiazide had precipitated this episode was supported when, several weeks later, Mr. A again consumed large quantities of liquids while continuing to smoke heavily, was rehospitalized, but was asymptomatic this time and had a normal serum sodium level.

It is not known why some patients with chronic schizophrenia drink excessive amounts of water, particularly during relapse, or why about 3% of those who do so develop hyponatremia (4). It is suggested repeatedly in the literature on polydipsia that the increased dopamine activity associated with schizophrenia perturbs the mechanism controlling thirst and/or stimulates excess secretion of antidiuretic hormone, leading to greater retention of water and dilution of sodium in serum (3). Neuroleptics and nicotine from heavy cigarette smoking (4) are also mentioned as possible contributing causes of hyponatremia.

Thiazide diuretics inhibit reabsorption of sodium in the kidney, causing loss of both sodium and water from serum. Impaired urinary dilution and inappropriate antidiuretic hormone secretion can also contribute to thiazide-induced hyponatremia (5). By drinking excess water, schizophrenic persons who take these diuretics can then further dilute serum sodium to life-threatening or lethal levels.

Excess water consumed by polydipsic schizophrenic patients should be considered a "drug" in a potential drug-drug interaction with any substance that alters water balance. The polydipsia diagnosis should be conspicuously noted in the charts of such patients, and a warning about prescribing thiazide diuretics should appear.

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Unexpected Intracerebral Pathology in Older Schizophrenic Patients

SIR: We wish to report a high frequency of unexpected intracerebral pathology in a group of older schizophrenic patients, most of whom were men. We obtained CT scans of 29 patients (27 men and two women) over age 55 during a longitudinal study (1). Patients with histories of degenerative brain disease, stroke, substantial alcoholism, or brain injury were excluded. Several of the scans exhibited lucencies suggestive of past cerebrovascular accidents as well as other pathology. The scans were examined by a neuroradiologist (M.T.B.) who was blind to information about the patients. If there was an obvious, well-defined cortical or subcortical lucency consistent with a past infarct, the patient was considered to have had a cerebrovascular accident. Ten of the patients (34%) had evidence of a probable past cerebrovascular accident, two had bilateral basal ganglia calcification, and one had extreme ventriculomegaly. Eight (80%) of the probable cerebrovascular accidents were lacunae, one was a moderate left parietal lesion, and one was a large subcortical lucent area involving the left lenticular and subthalamic nuclei. Four patients had diagnoses of type II diabetes mellitus and seven were hypertensive. There was no significant association of either of these risk factors with cerebrovascular accident in this group. Other risk factors (e.g., smoking, family history) were not systematically examined.

There were substantial clinical correlates of the CT findings in three of the patients: 1) the patient with a large subcortical infarct had severe right-side hemiparkinsonism that had been previously misdiagnosed as tardive dyskinesia, 2) one of the patients with bilateral basal ganglia calcification had severe tardive dyskinesia and cognitive impairment, and 3) a patient with a recent history of behavioral deterioration, originally attributed solely to a reaction to his mother's death, had severe ventriculomegaly and cognitive dysfunction. Subsequent longitudinal follow-up of this patient revealed progressive cognitive decline, and he was given a diagnosis of probable Alzheimer's disease in addition to schizophrenia.

Cerebrovascular disease occurs more frequently in older persons; nevertheless, a surprising number of these patients had probably had a cerebrovascular accident. We did not study age-matched normal control subjects, but past studies have estimated the rate of unsuspected infarction in older normal subjects (2) and in younger schizophrenic patients (3) as 2.5% and 5.5%, respectively. Further systematic investigation of patients in this age group is warranted.

Although most of the abnormalities observed in these patients were clinically silent, in three cases there were obvious and severe associated behavioral or neurological findings. Cerebral lesions may have gone unnoticed because the patients did not report symptoms and/or because signs and symptoms were misinterpreted by clinicians. The presence of dementia or extrapyramidal symptoms in otherwise normal persons usually prompts a search for CNS pathology. In this sample, however, neurological symptoms (especially extrapyramidal symptoms) and neuropsychological dysfunction were quite common, and appropriate neurodiagnostic evaluation had not been performed. These findings demonstrate the continued utility of CT scanning in patient assessment despite the development of higher-resolution, more expensive techniques such as magnetic resonance imaging.

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Safer Use of MAOIs

SIR: Sometime after the introduction of monoamine oxidase inhibitors (MAOIs) in psychiatric practice, it was discovered that tyramine-rich foods eaten during treatment with MAOIs could produce a potentially serious hypertensive crisis. After their initial removal from the market, MAOIs were returned a few years later with recommendations for reduced dosage and avoidance of food and beverages containing tyramine. Many practicing physicians became wary of prescribing MAOIs, and patients came to regard them as dangerous drugs. As interest in MAOIs began to increase, psychiatrists were warned not to prescribe them along with tricyclic antidepressants and never to add an amphetamine-like drug to the treatment regimen. The experience of our European colleagues in prescribing both MAOIs and tricyclics in the treatment of resistant depressions took a while to raise our level of awareness of the relative safety of this practice. This fact has not yet found its way into the *Physicians' Desk Reference.*

The MAOIs are excellent antidepressant and antipanic drugs and are generally without anticholinergic, cardiotoxic, or sedative side effects. For patients with atypical depression (hypersomnia and hyperphagia), those who cannot tolerate anticholinergic side effects, the elderly, and medically compromised patients, MAOIs are often the drugs of choice. However, legitimate concerns about the risks of hypertensive crisis still exist; patients sometimes "cheat" on the diet or accidentally ingest one of the forbidden foods. While a majority of patients seem not to suffer ill effects, some do experience hypertensive crisis. The hypertension can be severe and can cause intracerebral bleeding. Haft and Litterer (1) in 1984 discussed the use of nifedipine for rapid treatment of hypertension, and Clary and Schweitzer (2) reported on two cases of MAOI hypertensive crisis treated with sublingual nifedipine. In the past, hypertensive crises have been treated with intravenous nitroprusside drip or intravenous injection of phentolamine. These treatments obviously necessitated a trip to a hospital emergency room, loss of time in the initiation of treatment, and considerable expense. In recent years the treatment of choice for MAOI hypertensive crisis appears to be sublingual nifedipine.

Sublingual nifedipine generally works in 5–10 minutes, very effectively lowers blood pressure, and does not appear to have serious side effects. Absolute reduction in blood pressure with nifedipine tends to be in direct proportion to pretreatment blood pressure levels. In my practice, after determining that an MAOI is indicated, I review the dietary restrictions with the patient and provide him or her with a printed copy of the diet. Further, I discuss the symptoms of a hypertensive reaction and underscore the seriousness of the situation. I then prescribe about six 10-mg capsules of nifedipine with instructions to leave one in the car, one in the office, one in the purse, etc. and tell the patient that in the event of a hypertensive headache, he or she should bite into the capsule and place the contents under the tongue. The patient is instructed to seek emergency medical treatment if the headache does not disappear or improve within 5–10 minutes.

Prescribing nifedipine along with MAOIs significantly decreases the risk of intracerebral bleeding. It essentially places accepted emergency room treatment in the patient's pocket, reduces the initiation time of treatment, and thereby greatly reduces risk. Physicians who have formerly been reluctant to prescribe MAOIs because of the risk of hypertensive crisis can now feel much more comfortable and avail themselves and their patients of this very useful group of antidepressant medications.

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Severe Hair Loss Associated With Fluoxetine Use

SIR: I would like to report the following case.

> Ms. A, a 53-year-old unemployed woman, reported having had severe obsessions and compulsions since her early 20s. She feared touching items in her house because of possible contamination and had extensive ordering and checking rituals. Much of her day was spent repeating activities until they "felt right." If she resisted her rituals, she became severely anxious and did not feel well until she eventually gave in to them. Ms. A felt that she could not eat unless "everything had been done exactly correct and in order," and as a consequence she weighed 75 lb, which was 30 lb under her ideal body weight. Her score on the Yale-Brown Obsessive-Compulsive Scale was 26, and her Maudsley Obsessional-Compulsive Inventory score was 22. Both of these scores indicated severe disability secondary to her obsessions and compulsions. Her Beck Depression Inventory score was 21, indicating moderate depression.
>
> Previous treatments for her obsessive-compulsive disorder had included more than two decades of psychodynamic psychotherapy and trials of medications such as diazepam, alprazolam, imipramine, and nortriptyline. Findings from a medical work-up were normal, and the patient was started on a regimen of fluoxetine, 20 mg each morning (1–3). The dose was raised over the next 5 weeks to 40 mg twice daily, and after 2 months she began behavior therapy with exposure and response prevention. Over the next 5 months, she lost 3 lb but complained of no side effects of the fluoxetine except for mild "shaky hands." After about 5 more months, Ms. A reported that "huge clumps of hair" were coming from her head whenever she brushed her hair. Examination showed a general thinning of her hair, and in a number of areas, the skin of her scalp could be clearly seen through the remaining fine hairs. A complete medical work-up, including thyroid function tests, CBC, and chemistries revealed no other cause for the hair loss. She was not taking any other medication concomitantly. She took great pride in her shoulder-length hair and was very distressed, so she discontinued the fluoxetine despite feeling that it had helped her somewhat.
>
> Ms. A noted some minimal hair loss even 2 months after discontinuing fluoxetine. At 4-month follow-up, hair loss had stopped, and hair was growing back. After 6 months, her hair had returned to normal.

A computerized Paper Chase literature search revealed no previously reported cases of hair loss or alopecia related to use of fluoxetine. In a multicenter trial of about 600 patients who received fluoxetine, alopecia was listed as a side effect in less than 1% of the patients, but a causal relationship was not determined (personal communication, Dista Pharmaceutical Co., November 1990). Severe hair loss may be an uncommon but potentially distressing side effect of fluoxetine.

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Clozapine as an Alternative Treatment for Neuroleptic-Induced Gynecomastia

SIR: Commonly used neuroleptics, in contrast to most other psychotropic drugs, are known to stimulate prolactin secretion (1), which may lead to gynecomastia and even galactorrhea in some patients (2). Meltzer and Fang (3) observed 3.2-fold and 3.8-fold increases of prolactin in 27 schizophrenic men and women, respectively, 72 hours after initiating neuroleptic treatment. We report a case in which a patient who developed gynecomastia after receiving classical neuroleptics recovered from this side effect after switching to clozapine.

> Mr. A was a 55-year-old patient suffering from schizophrenia, residual type. As an outpatient, during one winter he needed considerable neuroleptic medication: 15 mg of haloperidol, 175 mg of levomepromazine, and 200 mg of thioridazine daily, as well as biperiden. At the end of February, during a physical examination, the treating physician observed bilateral gynecomastia without galactorrhea. The patient's prolactin level was 23.4 ng/ml (normal values in men=2–10 ng/ml), and his plasma haloperidol concentration was 4.4 ng/ml. Because of these findings and because his clinical picture had worsened during the last 6 months, it was decided to decrease the neuroleptic medication. Thioridazine and haloperidol were stopped in the middle of April, biperiden on April 28, and levomepromazine on May 2. Clozapine was slowly introduced in mid-April, and a final daily dose of 400 mg was reached on April 29.
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> On May 3 Mr. A's prolactin level (2.2 ng/ml) was within the normal range. However, he was hospitalized 2 weeks later because of an increase in several symptoms: loss of appetite and weight, psychomotor agitation, incoherence in speech and behavior, anxiety, and neglect of grooming and work.
>
> On July 5, all symptoms of gynecomastia had disappeared in parallel with the return to normal of the prolactin level. In the next few weeks, the global clinical picture of the patient improved, as did his sleep, weight (gain of 6 kg), and anxiety. However, he still presented logorrhea and increased motor activity. His hematological measures,

checked weekly during clozapine treatment, remained within the normal range.

This case demonstrates, as previously shown, that prolactin levels rapidly return to normal after neuroleptics are stopped. Indeed, Meltzer and Fang (3) observed that after patients stopped neuroleptic treatment, their prolactin levels were normal within 48–96 hours. The search for neuroleptics that are devoid of extrapyramidal side effects and that do not induce tardive dyskinesia has gained much interest. Clozapine is such an atypical neuroleptic, and it is known to have no effect (4) or only a small, transient effect (5) on prolactin levels. As demonstrated in this case, clozapine can be used as a substitute for other neuroleptics that are potent stimulators of prolactin secretion, especially in a situation where the patient presents side effects related to this hormonal change and consequently incurs a greater risk of developing breast cancer.

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Thyroid Function and Phototherapy in Seasonal Affective Disorder

Sɪʀ: There is a well-known association between thyroid dysfunction and abnormalities of mood (1, 2). One of the most consistently observed findings in patients with primary affective disorder is that a variety of antidepressant treatments cause limited but substantial decrements in thyroid function (1, 2). In particular, treatment with tricyclic antidepressants, ECT, carbamazepine, and lithium causes substantial decreases in measures of T_4 and T_3 with or without changes in thyrotropin (TSH).

Phototherapy has been documented as an effective treatment for seasonal affective disorder (3). We were therefore interested in determining whether light treatment for winter depression would be associated with alterations in thyroid function. Although light does not specifically affect the thyroid, phototherapy, by alleviating depression, may alter thyroid function.

Fourteen subjects, six male and eight female, whose mean±SD age was 42.4±12.2 years, consented to participate in a treatment program. All received 2 weeks of light treatment administered for 1 hour between 6:00 and 7:00 a.m. at an intensity of 5000 lux. All subjects fulfilled the *DSM-III-R* criteria for seasonal affective disorder as determined by a structured interview in which the Schedule for Affective Disorders and Schizophrenia—Lifetime Version (4) was used. Blood was drawn just before and at the completion of 2 weeks of light treatment. All subjects were medication free for the duration of the trial. Standard radioimmunoassays were used for measurement of T_4, T_3, T_3 resin uptake, and TSH. The free T_4 index (FTI) was calculated as the product of the T_4 and T_3 resin uptake measures.

There was no significant difference between the end of light treatment and baseline in mean±SD serum levels of T_4 (117.8±21.4 nmol/liter versus 113.5±22.5 nmol/liter; normal=51–142); T_3 (2.3±0.5 nmol/liter versus 2.1±0.4 nmol/liter; normal=1.1–3.2); T_3 resin uptake (0.30±0.02 versus 0.30±0.02; normal=0.25–0.35); TSH (3.4±2.7 mU/liter versus 3.6±2.9 mU/liter; normal=0.5–4.5); or FTI (33.6±4.6 versus 33.2±4.9; normal=13–50).

Eleven of the 14 patients had an antidepressant response to phototherapy. Reanalysis of the data excluding data on the three nonresponders did not substantially alter the findings.

Phototherapy had no significant effects on thyroid function in our group of patients with seasonal affective disorder. It may be that more than 2 weeks is required before changes in thyroid function with light treatment can be observed in these tests. The change in thyroid function with other antidepressants occurred after 4–6 weeks of treatment (2).

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A Patient's Psychotic Interpretation of a Drug Side Effect

Sɪʀ: We would like to report the case of a patient with neuroleptic-induced akathisia who developed a delusion that external forces were controlling his legs, which represented a psychotic interpretation of this side effect.

> Mr. A, a 34-year-old man with a 6-year history of paranoid schizophrenia and poor compliance with regimens of oral medications, was admitted to the hospital with an acute paranoid psychosis after missing two fluphenazine decanoate injections. As on previous admissions, he had delusions focused on his "evil" brother's "immoral" sexual behavior. On the evening before admission, Mr. A had clipped all the photographs from his brother's pornographic magazine and set them on fire in his bedroom wastebasket.
>
> On admission Mr. A was started on fluphenazine, 10 mg/day p.o., and his psychosis initially improved. However, after several weeks he complained of restlessness and showed psychomotor agitation consistent with akathisia.

He was then started on propranolol, but before he could respond, it was noted that he was preoccupied and more socially isolated and withdrawn. He revealed his belief that an outside force—possibly related to his brother—was controlling his legs. He believed that through mental control he could wrestle with and overcome the force's effects, although he refused to divulge his methods. After his dose of propranolol was increased to 80 mg/day, the akathisia and the psychotic ideas about control of his legs simultaneously resolved without a change in his neuroleptic medication. As his psychosis improved, on several occasions Mr. A referred to the restlessness as a side effect of his neuroleptic medication.

Akathisia is reported to occur in 20% of patients receiving neuroleptic medication (1). Van Putten found that development of akathisia was a major reason for refusal to take antipsychotic agents (2), and Van Putten et al. described "phenothiazine-induced decompensations" in which akathisia was associated with exacerbations of psychosis that were similar to the original symptoms (3). However, we were unable to find cases in the literature of psychotic interpretations of akathisia. Although akathisia has been cited in association with suicidal (4) and homicidal (5) ideation, it is unclear whether this is a result of the severe restlessness itself or is associated with similar psychotic interpretations of the meaning of the akathisia. This appears to be the first case report of a delusion of external control resulting from a neuroleptic-induced akathisia.

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Sun Gazing by Patients With Tourette's Disorder

SIR: We greatly appreciate the case report by Peter S. Kamp, M.D., and associates on retinopathy in psychotic adults who gaze at the sun (1). We would like to cite another psychiatric condition that causes sun gazing and could lead to retinopathy, although such damage was not documented in these two patients.

Ann, a child of above-average intelligence, was 5 years old when she was first given a diagnosis of Tourette's disorder. She presented with multiple moderate vocal and motor tics, which classically waxed and waned and changed sites with varying degrees of frequency and severity. She also had visual-motor-perceptual problems and mild symptoms of attention deficit hyperactivity disorder. There was a family history of tics in her relatives, but her medical history was otherwise unremarkable. Ann did not have any learning difficulties or interpersonal problems with peers. The tics were not severe enough to be treated medically until she was 8 years old, when the tics worsened and more obsessive-compulsive symptoms developed. At age 5 she had developed a behavior of looking at lights and the sun. It was not clear whether this represented a compulsion to look or a "rationalization" for a tic that forced her gaze upward. Fortunately, this light- and sun-gazing behavior lasted only a few months and has not returned in 5 years of follow-up. Ophthalmologic consultation did not reveal any signs of retinopathy.

John, a 14-year-old boy, had been given a diagnosis of Tourette's disorder when he was 6 years of age. The Tourette's disorder, as well as obsessive-compulsive disorder, had been treated with a variety of medications. The patient reported that from age 10 to age 14 years, he had had a compulsion to look at the sun "until my vision gets black and there is sharp pain in my eyes." This was one of many compulsions that consisted of repeating an act—flexing muscles, touching hot objects, etc.—until it was painful. The symptoms decreased, but when he was seen at age 14 years, John was referred for ophthalmologic consultation to rule out retinopathy and to obtain sunblock glasses. He was lost to follow-up, so results of the retinal evaluation are unknown.

A review of the literature and a discussion with the Tourette Syndrome Association (personal communication, June 1990) did not reveal any previous reports of retinopathy or sun gazing in patients with Tourette's disorder. Thus, we would like to add Tourette's disorder to psychotic disorders as a potential cause of sun gazing and retinopathy (1). In addition, we suggest that clinicians also consider the spectrum of tic disorders and obsessive-compulsive disorder in this respect, because of a suspected genetic inheritance linkage (2). Since retinal damage can be easily prevented by eyeglasses that block ultraviolet radiation (personal communication, G.A. Chrousos, June 1990), we echo Dr. Kamp and associates' plea for physicians, families, and patients to be aware of this potentially serious complication and the need for ophthalmologic consultation.

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A Variant of the Syndrome of Subjective Doubles

SIR: In reviewing the literature on delusions of substitution, Singer (1) could discern two forms of the syndrome of subjective doubles: 1) the Capgras type, in which unseen doubles are believed to be active in the environment, and 2) an autoscopic type, first described by Cristodoulou (2), in which the patient recognizes physically identical doubles of himself in persons around him.

We present another variant of the syndrome of subjective doubles with an unusual disturbance in experiencing time.

Mr. A, a 19-year-old student, was admitted to a clinic because of disturbing auditory hallucinations and suicidal ideation. On admission he showed blunted affect and reported voices commenting on his behavior, audible thoughts, and delusions of thought broadcasting and thought withdrawal—experiences of influence, yet without manifest behavioral aberrations. The next day he became nervous and agitated. On questioning he described the impression that he had already been on this ward. He was puzzled and irritated because he was conscious of the fact that this could not be true. He reported an overwhelming sense of familiarity with his surroundings, although he could not cite any concrete similarities to previous experiences. He felt that the individuals on the ward—patients and male personnel—were also familiar and that they had something in common with him and with one another which he could not explain. Later on he lost all sense of reality and expressed the conviction that all of these men were in fact the same person (namely, himself) and that their different appearances were because of their different ages. There was the Mr. A of yesterday, the Mr. A of tomorrow, and the Mr. A of the day after tomorrow. All of these were his own person at different times; the oldest was going to die, and then a part of himself would be dead.

Findings from a neurological examination, routine laboratory investigation, CSF, brain scan, EEG, and a battery of psychological tests were all normal. We diagnosed paranoid schizophrenia (*DSM-III*) and treated Mr. A with neuroleptics. After improvement and discharge he tried unsuccessfully to continue his studies. He was readmitted with a depressive syndrome after the suicide of his father a few months later. He was still taking the neuroleptics prescribed after the first discharge. On the second admission neither first-rank symptoms nor paranoid misidentifications could be detected.

This case differs from the known variants of the syndrome of subjective doubles in that 1) the doubles were not just believed in, as is true in Capgras' type, and 2) there was no physical identification with them, as there is in Cristodoulou's type. Otherwise, there are striking similarities to the autoscopic phenomena and especially to the deuteroscopic type, namely, the experience of a psychological but not a physical duplication of one's real self (3).

Berson (4) postulated that there are common factors between the Capgras and autoscopic phenomena. We think that the feelings of dé jà vu, or dé jà vecu, that initiated the symptoms in our patient and in Cristodoulou's original patient are identical to the feeling of "belonging" considered by Damas Mora et al. (3) to be the most significant feature of autoscopy. It seems that feelings of an "ultimate familiarity" constitute a cardinal common factor in the development of these phenomena and could offer, beyond the fanciful terminology, the conceptual framework for a more thorough understanding and a more simple classification.

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Dissociation in Endogenous Psychosis

SIR: Dissociation phenomena were major areas of clinical investigation during the time of Janet (1). Subsequently, there has been a decline of interest in these clinical syndromes, although there has been no evidence to suggest that the incidence of the phenomena has in any way diminished since that time (2).

Conversion symptoms involving the sensorimotor system are frequently seen in patients with somatic diseases (3) and psychiatric disorders (4). Shalev and Munitz (5) reported a case in which conversion was associated with paranoid psychosis. The combination of dissociation phenomena and endogenous psychosis is not frequently reported in the literature. We report two cases from north India in which patients with endogenous psychosis also had dissociation symptoms.

Ms. A, a 52-year-old married woman, had a diagnosis of bipolar affective disorder according to the *DSM-III-R* criteria. At the age of 45 years she had had her first attack of endogenous depression. This episode was characterized by sadness, weeping spells, suicidal ideas, insomnia, negative ideas, and psychomotor retardation. Since then she had been having one or two attacks of mania and depression every year. The manic attacks were characterized by increased psychomotor activity, inappropriate euphoria, and insomnia. She did not respond to lithium prophylaxis. She had been hospitalized three times, once for depressive illness and twice for manic excitement. After recovery from the third attack of depression, Ms. A began to have episodes of unconsciousness during which she would become unresponsive; these lasted for a few minutes to a few hours. Twice during these episodes, EEGs failed to show seizure activity. The episodes could be induced by suggestion, and she had partial amnesia for events during them. The episodes always occurred in periods of severe depression; she never experienced them during manic psychosis and symptom-free periods.

Mr. B, a 23-year-old unmarried man, was an outpatient who had a diagnosis of schizophrenia according to the *DSM-III-R* criteria. His first attack of schizophrenia had occurred when he was 16 years old. His illness was characterized by psychomotor excitement, violence, inappropriate affect, and suspiciousness. The symptoms did not remit after the first attack, and although he had been given regular maintenance injections of fluphenazine decanoate, he had been having one or two acute exacerbations every year. After improving from the second attack of the illness, he started to have episodes of unconsciousness lasting from 15 to 30 minutes, during which he would close his eyes and clench his teeth. He remained responsive to deep and painful stimuli but did not respond to verbal stimuli. He experienced three to five of these episodes a week, and they could be induced by suggestion. Twice during such episodes, EEGs did not show evidence of seizure activity.

Both of these cases were characterized by concurrent endogenous psychosis and dissociation. The presence of dissociation in these patients could not be correlated with specific life events that were meaningful to them. Could the episodes of dissociation have been the result of release of psychotic anxiety?

It is interesting to note that for each of these patients there was a time lag following the first episode of psychosis before the dissociation symptoms appeared. It is possible that in chronic patients, tolerance of stress becomes much less, and in these patients dissociation was precipitated by very minor stresses that could not be elicited by our repeated interrogation.

This report clearly shows that neurotic phenomena are not only the domain of neurotic patients but that psychotic patients can also develop these symptoms.

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Organic Mental Disorders and *DSM-IV*

Sir: In this journal (1) and elsewhere (2), Z.J. Lipowski, M.D., has characterized a proposal to eliminate the category of organic mental disorders in *DSM-IV* as "idiosyncratic" and likely to "create confusion" and "impede communication." This proposal was originally formulated by Robert L. Spitzer, Janet B.W. Williams, Michael B. First, and Kenneth S. Kendler (3) and arose in response to concerns among work group members and experts in the field that the organic/nonorganic distinction had become anachronistic. The final proposal, presented by the *DSM-IV* Work Group on Organic Mental Disorders (4), has two main goals. The first is to facilitate differential diagnosis by grouping phenomenologically similar syndromes or disorders in the same major diagnostic class. Thus, the clinician, in determining the differential diagnosis of depressed mood, would find within the class of mood disorders what in *DSM-III* and *DSM-III-R* were called organic mood disorder and drug-induced mood disorders. A natural consequence of this approach is to retain together the traditional (pre-*DSM-III*) organic mental disorders of delirium, dementia, and amnestic disorder within the overall rubric of cognitive impairment disorders.

The second goal is to replace the term "organic" with a term that is more precise and less likely to perpetuate the false implication that the "nonorganic" disorders lack a significant biological component in their etiology. We believe that the term "secondary," as in "secondary mood disorder," more clearly conveys the *DSM-III-R* and *ICD-10* constructs, namely, a disturbance of mood that is judged to be secondary to a nonpsychiatric medical disorder. Dr. Lipowski believes that any confusion in the meaning of the term "organic" can be solved by the *ICD-10* statement that the term merely means "that the syndrome so classified can be attributed to an independently diagnosable cerebral or systemic disease." We doubt that this or any other attempt to redefine "organic" will succeed in overcoming the unfortunate historical baggage that the term has accrued. In fact, the wording of the *ICD-10* statement is equivalent to the way in which we are proposing that the term "secondary" be used.

The introduction of any change in psychiatric classification and terminology has the potential for creating short-term confusion, since users have to learn new concepts. In this case, we feel that the long-term benefits in clarity and in improved differential diagnosis, on balance, justify what we regard as an important step forward in our nosology. With several of our colleagues on the Task Force on *DSM-IV* and the Work Group on Organic Mental Disorders, we are currently preparing a paper that makes a complete presentation of the proposal, including a historical review, as well as responses to critiques of the proposal.

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Dr. Lipowski Replies

Sir: Dr. Spitzer and associates object to my critique of the proposed abolition of the category of organic mental disorders in *DSM-IV*, yet they fail to provide any convincing reasons in support of this proposal. A term means no more and no less than its definition specifies and this applies to the term "organic" in the present context. I have just received the 1990 draft of chapter 5 of *ICD-10*, which contains a separate section called "Organic, Including Symptomatic, Mental Disorders." It is introduced by a statement that "this section comprises a range of mental disorders grouped together on the basis of their having in common a demonstrable aetiology in cerebral disease, brain injury, or other insult leading to cerebral dysfunction" (p. 30). It is further stated that "the term 'organic' means no more and no less than that the syndrome so classified can be attributed to an independently diagnosable cerebral or systemic disease or disorder. The term 'symptomatic' refers to those organic mental disorders in which cerebral involvement is secondary to a systemic extracerebral disease or disorder" (p. 30).

These quotations make it clear that in *ICD-10*, the organic diagnostic category is based on etiologic and not on descriptive considerations. The proposed changes in *DSM-IV* are completely at variance with this approach—one that prevails worldwide—and would result in needless difficulties in communication. I believe that such changes should not be made lightly and without a wide debate about their alleged usefulness. Many colleagues, American and European, have privately expressed agreement with my position on this point, and I hope that they will state their views publicly. Liaison and geriatric psychiatrists see the majority of patients with organic mental syndromes and would be particularly affected by the proposed changes, since they have to communicate intelligibly with their nonpsychiatric colleagues.

Prior to *DSM-III* the area of organic mental disorders had been plagued by a conceptual and terminological muddle that contributed to the neglect of those disorders by researchers and impeded clear communication. The literature of the past decade suggests that this situation has improved considerably. It would be unfortunate if *DSM-IV* reversed the clock in this regard.

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Plasma Prolactin Levels and Cocaine Abuse

SIR: Conrad M. Swartz, Ph.D., M.D., and his associates reported that patients "who claimed to have stopped using cocaine less than 6 months before admission after having used it at least once a week for 6 months or more" did not have abnormally high serum prolactin levels (1). They contrasted their findings with data obtained at our clinical research center (2, 3) and with other reports that hyperprolactinemia is a concomitant of cocaine abuse and dependence (4, 5). Dr. Swartz and his colleagues stated that "serum prolactin levels were determined with the use of a radioimmunoassay kit (Diagnostic Products, Los Angeles); the normal range for men is 0–15 ng/ml." However, no information was provided about the sensitivity of the prolactin assay, nor were intra-assay and interassay coefficients of variance reported. Were prolactin assays carried out in duplicate, and were prolactin values for normal subjects measured in the authors' laboratory? In table 3 the authors reported that one patient (number 22) had a serum prolactin level of 1 ng/ml, and three other patients (numbers 21, 8, and 3) had serum prolactin levels of 2 ng/ml. Does the assay used by the investigators reliably detect such low prolactin levels? Finally, is a value of 0 ng/ml considered normal for men? It would be most helpful if the authors could further describe the precision, accuracy, reliability, and repeatability of the prolactin assay they used in their study.

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Dr. Swartz Replies

SIR: The full name of the radioimmunoassay kit we used was the "Prolactin Double Antibody, With Human Serum Calibrators" from Diagnostic Products Corp. of Los Angeles. In our laboratory, with this kit, the intra-assay and interassay coefficients of variance are 8.22% and 10.71%, respectively. These are comparable to Dr. Mendelson and associates' figures (1) of 4.1% and 11.1%, respectively. They are a little higher than the figures given in the package insert (4.4% and 8.6%, respectively), but not enough to have a substantial influence on our data or influence our conclusions.

All sample assays were performed in duplicate. We periodically measure the accuracy of our assay against samples mailed to our laboratory from an independent testing bureau. They advise us of the actual serum prolactin levels of these samples a couple of months after we assay them and record the results; our mean absolute error has been 4.4%. The detection limit of the assay is 1.4 ng/ml. Of course, apparent levels below this are not reliably distinguishable, and so the apparent levels of 0 and 1 ng/ml merely represent serum prolactin levels at or below 1.4 ng/ml. In view of the severe space limitations on our report, we simply reported the apparent serum prolactin levels, to avoid discussion of relatively low-priority methodological details, and for the same reason, we left out the details we have provided here.

All of the questions we have just answered concern our own procedures. The question about the lower limit of normal for serum prolactin in men is somewhat philosophical, because absence of the milk-production hormone prolactin in men is not known to have any detrimental consequences. Further, the package insert noted that independent laboratory testing of 90 normal adults with this assay suggested that it is normal for men to have serum prolactin levels so low that they are undetectable. Although our prolactin detection limit of 1.4 ng/ml is lower than the limits reported by Dr. Mendelson and associates—4.6 ng/ml (1) and 5.8 ng/ml (2)—such apparent differences in sensitivity do not seem to be related to our observation that high serum prolactin levels did not occur during cocaine abstinence in our patients.

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Combined Treatment With Lithium and Carbamazepine

SIR: Keith G. Kramlinger, M.D., and Robert M. Post, M.D., studied additive and opposing effects of lithium and carbamazepine on hematologic and thyroid function (1). Our group of investigators noted an increase ($p=0.003$) in WBC count from 6458 to 9365 cells/mm^3 when we added lithium to carbamazepine (2). We noted no important clinical or laboratory differences in thyroid function between patients taking lithium alone and those taking it with carbamazepine (3).

The methods and statistics used by Drs. Kramlinger and Post complicate interpretation of their data. First, they did not define the placebo period; it may have been as short as 1 week (1, figures 1 and 2). To study placebo effect better, the duration of placebo and drug periods should match. Also, the authors could have tested the additive effect of lithium on carbamazepine by adding placebo to carbamazepine.

Second, the range of duration of carbamazepine treatment was more than just an order of magnitude. For some patients the first 3 weeks of combined treatment were compared with the last 3 weeks of long-term carbamazepine treatment (300 or more days), while for others the first 3 weeks of combined treatment were compared with the last 3 weeks of very short-term carbamazepine treatment (sometimes less than 3 weeks).

Third, the authors' method of data analysis increases the likelihood of reaching a p value of 0.05, because they did not correct for the many similar statistical tests. Their findings may be premature. They did not use the Bonferroni principle for multiple comparisons (dividing 0.05 by the number of tests used) in their multiple two-tailed (?), paired t statistics. Repeated measures analysis of variance with post hoc testing would have reduced the need for so many t statistics. There were three paired t statistics (placebo versus carbamazepine, placebo versus carbamazepine-lithium, and carbamazepine versus carbamazepine-lithium) for each hematologic variable (WBC, lymphocytes, neutrophils, eosinophils, basophils, monocytes, RBC, and platelet count), which yields a Bonferroni p value of 0.002 (0.05/24). None of the t statistics in the first paragraph of the Results section reached this value.

In the second paragraph of the Results section, some t statistics reached a p value of 0.002 (WBC count during the last 3 weeks of carbamazepine versus the first 3 weeks of carbamazepine-lithium, and lithium potentiation of neutrophils). No t statistics in paragraphs 3 and 4 were significant.

The lithium-induced quantitative increase in WBC count does not necessarily mean that the cells were qualitatively better. Did the subjects have fewer or less serious infections when lithium was added to carbamazepine?

In the thyroid analysis, the authors divided patients into three groups and compared findings on T_4, free T_4, T_3, thyrotropin (TSH), and thyroxine-binding globulin. The Bonferroni p value is 0.003 (0.05/15). Carbamazepine lowered T_4 and free T_4 below baseline values; there was further drop in T_4 when lithium was added to carbamazepine. They concluded that adding carbamazepine to lithium does not increase the risk for hypothyroidism over that with lithium alone.

The opposing effects of carbamazepine and lithium on water regulation (4) warrant attention. The authors placed little emphasis here, but their group has studied the effects of carbamazepine on electrolytes (5). The least appreciated side effect of lithium-carbamazepine on water regulation occurs when lithium alone is stopped. We have found repeatedly that hyponatremia may occur, which is prevented earlier by the lithium (4).

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Dr. Post and Dr. Kramlinger Reply

SIR: The letter of Dr. Vieweg and associates raises several issues regarding the clinical laboratory findings on the combination of lithium and carbamazepine in our study. We are perplexed by several of their statistical criticisms. Our findings replicate and extend the work of several other investigators in the field, including their own. Thus, whatever arguments they have about our statistical analyses, it is difficult to support their view that our "findings may be premature." Our manuscript was reviewed not only by several in-house statisticians but also by a statistical expert from the *Journal*, who stated that he had no problem with this use of multiple t tests. Moreover, Ware et al. (1) have indicated that "multiple comparison and selection effects can yield misleading t values. Full reporting and statistical adjustment can help correct for these misleading values, but the choice of an error rate—per statement, per question, or per investigation—seems arbitrary. Studies with low statistical power can lead to unjustified decisions about therapies and other medical results." One should be equally alert for type II errors in this regard.

As we reported, neutrophils and platelets but not other hematologic indices increased when the patients were taking lithium, which is consistent with much of the clinical and preclinical data (2). There was no relation between the duration of carbamazepine therapy and the degree of change evoked by lithium; onset of lithium treatment provided the focal point of our analysis. Although Dr. Vieweg and associates raise the issue, it is clear that the qualitative functioning of WBC in relation to infection during carbamazepine treatment was not addressed in our study and requires quite a different set of methods. However, we have no evidence, either, on the basis of numbers of cells remaining and unsystematic clinical reports of infections, to presume that a problem would exist in this area.

In relation to thyroid indices, in spite of the greater drop in

T_4 when lithium was added to carbamazepine in our series of patients, we did not find any greater increase in TSH with this combination than we had observed in a substantial series of patients studied while taking lithium alone. This finding, together with the additional report by Dr. Vieweg and colleagues that there were few laboratory differences in thyroid function in their patients (reference 3 in their letter), appears to support the notion that the combination may not be more thyrotoxic than lithium alone, although this needs direct confirmation in a larger epidemiologically based study.

Our data do not directly address the potential of lithium for reversing carbamazepine-induced hyponatremia, as no patient in this series had clinically substantial hyponatremia. Lithium did not increase serum sodium levels that were already in the normal range when the patients were taking carbamazepine, although Dr. Vieweg and associates reported a lithium-induced increase in three patients with hyponatremia who were taking carbamazepine (reference 4 in their letter). Lithium may prove to be protective of carbamazepine-induced hyponatremia, as has been reported for demeclocycline (3).

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ROBERT M. POST, M.D.
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Physical and Sexual Abuse Histories of Male Psychiatric Patients

SIR: The article "Sexual and Physical Abuse Histories and Psychiatric Symptoms Among Male Psychiatric Outpatients" by Chester Swett, Jr., M.D., and associates (1) is a welcome addition to the literature on abuse of males. The finding that almost half of their subjects reported a history of sexual and/or physical abuse and that these same men had high levels of psychiatric symptoms emphasizes how important it is to take detailed and careful histories from male patients. I would like to comment and expand upon just the dimension of sexual abuse in the authors' findings and conclusions.

In my report of 14 men who had been sexually abused as boys and/or sexually assaulted as adults (2), I found that in only two cases was the abuse the chief complaint at the time of initial consultation. Many did not disclose the abuse until well into therapy, and some of these men—especially the homosexual men—did not even realize that they had been abused. None of them had told anyone about the abuse at the time of its occurrence and only four had told someone else before they told me. In addition to the feelings of shame and self-blame, the common defense mechanisms in these men were repression, denial, and normalization of the trauma.

This secrecy and silence are in keeping with the underreporting of male sexual abuse in North America. The finding by Dr. Swett and associates of an overall rate of 13% for sexual abuse is higher than the 6% found in Finkelhor's survey (3). This may reflect, as the former authors suggested—and apart from the different survey designs—a higher rate of sexual abuse among male outpatients than among the general population. But it might also suggest a greater degree of male candor and social permission for men to report such events in the years between the two studies.

Dr. Swett and associates urged consideration of the diagnosis of posttraumatic stress disorder (PTSD) for patients with histories of abuse. I concur wholeheartedly. Three of my 14 patients had symptoms of chronic PTSD, with recurrent memories of the sexual assault that intruded into consciousness, intermittent nightmares, and sporadic "psychic numbing." An additional four men gave histories highly suggestive of acute PTSD immediately after the childhood abuse, with flashbacks, partial amnesia, hypervigilance, sleep disturbance, feelings of detachment, and startle responses. All of these men—boys at the time—had suffered in silence.

Because of the high degree of mistrustfulness of adult men (present in half of my 14 patients), the marked amount of ambiguity about sexual orientation, and internalized homophobia, there are obviously adult male survivors of sexual abuse who will not easily tell male clinicians about what has happened to them. In addition, like Dr. Swett and associates, I have found that abused men talk more easily about having been physically assaulted than sexually assaulted (4). We male psychiatrists have a responsibility not only to increase our knowledge about this subject but to heighten our empathic sensitivity when interviewing this group of patients. Given the authors' findings, our medical students and residents, especially the men, also need more teaching, both didactic and by example, about assessing their male outpatients.

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Dr. Swett Replies

SIR: Dr. Myers has experience and data that corroborate ours. Prior findings on female inpatients (1) and outpatients (2) have now been extended to include men. The physical and sexual abuse of men needs to be studied in a variety of different settings in order to round out our knowledge.

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ical and sexual abuse and severity of symptomatology in women psychiatric outpatients. Am J Orthopsychiatry 1990; 60:412–417

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Need for Routine Medical Screening of Psychiatric Patients

Sɪʀ: In "Treatment of Hyperprolactinemia in Major Depression" (1), Suzanne Holroyd, M.D., and Mitchell J. Cohen, M.D., discussed a 31-year-old woman treated for 5 months for depression that did not respond to various psychopharmacologic and somatic interventions. A diagnosis of hyperprolactinemia, secondary to a pituitary microadenoma, was made only after referral and a "review of systems," even though the patient had had amenorrhea and galactorrhea for 9 months.

It is unfortunate that the patient did not initially consult a gynecologist instead of the referring psychiatrist. As not only a psychiatrist but also a gynecologist, I am certain that any competent gynecologist would have strongly suspected the diagnosis after obtaining the usual, routine gynecologic history during the patient's initial visit.

This case clearly demonstrates that a screening medical history is essential for all patients with psychological symptoms and is not necessarily reserved for patients with "refractory major depression." Taking a routine history is an obligation of the psychiatrist, who, lest it be forgotten, is a medical doctor first!

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Reprints of letters to the Editor are not available.

APA Official Actions

APA Council Reports

At the fall component meetings of the American Psychiatric Association in Washington, D.C., on Sept. 12–16, 1990, the APA councils heard reports from their components. Following are summaries of the activities of the councils and their components.

The Council on Addiction Psychiatry

Roger E. Meyer, M.D., Chairperson

The Council on Addiction Psychiatry, a newly established component, has a strong commitment to providing psychiatric leadership in the growing field of prevention and treatment of addictive disorders. The council will provide guidance to the Association in formulation of policy on addictive disorders to benefit the large number of Americans affected by them, will increase interest in and visibility of addictive disorders within psychiatry, and will provide liaison to the many government and voluntary organizations active in this field. Currently, one component reports to the council.

The *Committee on Training and Education in Addiction Psychiatry,* Robert Niven, M.D., chairperson, was recently established to evaluate the current status of training, both clinical and research, in addictive disorders; to make recommendations to the council for necessary changes in these training programs; to work toward optimal training programs for all psychiatrists; and to assist in producing psychiatrists with research expertise and academic credentials in this field. At its first meeting, on Sept. 13, 1990, the committee discussed potential tasks and identified relevant liaisons.

At its first meeting, in May 1990, the council voted to recommend that APA endorse the establishment of Added Qualifications in Addictive Disorders in Psychiatry, on the basis of the rationale and approach of the American Academy of Psychiatrists in Alcoholism and Addictions. In June 1990, the Joint Reference Committee and the Board of Trustees approved this recommendation. At its meeting in October, the Commission on Subspecialization also voted to approve this recommendation. The council's proposal was placed on the agenda of the Assembly.

During the fall component meetings, the council discussed preparations for the hearing on Added Qualifications in Addictive Disorders in Psychiatry during the meeting of the Commission on Subspecialization on Oct. 19, 1990, and the Assembly meeting on Nov. 9–11, 1990. The council felt it was important to bring this issue to the attention of the members of the Assembly before November to determine what questions, reservations, and concerns existed so they could be addressed in advance. To this end, several members of the council attended meetings of the area councils in September and October. The council also prepared a brief background document on this topic, which included a question-and-answer section. This document, circulated to the Commission on Subspecialization and the Assembly, addresses the high prevalence of drug and alcohol addiction and abuse in the United States and focuses on the high prevalence of comorbid psychiatric disorders in addicted patients; the enormous growth of scientific information in this field, including findings from epidemiology, neurobiology, basic behavioral and psychosocial investigations, and treatment and prevention research; and the recent involvement of organizations outside psychiatry in the treatment of addictive disorders.

The council considered the "Position Statement on Drugs of Abuse in Schools," prepared by the recently disbanded Committee on Drug Abuse. The council recommended that the Assembly and Board of Trustees endorse this position statement.

Because of its concern about the delivery of services for addictive disorders and reimbursement for these services, the council discussed the possible development of a committee on services and reimbursement in addiction psychiatry. This committee would evaluate the different types of available treatment, advise the council on important treatment issues affecting the practice of psychiatry, and monitor, evaluate, and advise APA on current and new funding mechanisms and problems, including adequate coverage under various funding schemes. Although the council recommended that APA establish such a committee, the Joint Reference Committee did not favor it and encouraged the council to form liaisons with the Council on Economic Affairs and the Council on Psychiatric Services to discuss ways in which APA might fully address these specific issues.

The council considered several documents concerning the legalization of drugs, including an Assembly action paper on this topic. The council recognizes the importance of studying this issue but opposes the legalization of drugs. Because of its biased position, the council recommended the establishment of a task force to develop a report outlining the scientific factors that would affect the decision to support or not support the legalization of drugs. This recommendation was approved by the Joint Reference Committee in October and will be presented to the Board of Trustees for its approval.

The council recommended that APA endorse a federal requirement for health warnings in advertisements for alcoholic beverages. This recommendation was approved by the Board of Trustees and was communicated to Congress by the Division of Government Relations.

During its first few months of operation, the council has already been busy. The council looks forward to addressing several important issues related to addiction psychiatry in the coming year, including continued efforts to establish Added Qualifications in Addictive Disorders in Psychiatry, programs for exchanging used needles and syringes for clean ones, and mandatory drug screening of medical staff. Additional components may be necessary to fully address the many research and clinical issues facing psychiatrists in the addiction field.

The Council on Aging

Jerome Albert Yesavage, M.D., Chairperson

The Council on Aging has had a productive year. Among the year's highlights were the upcoming decennial White House Conference on Aging in 1991 and the establishment of a formal working relationship with the American Association of Retired Persons (AARP) on issues pertaining to mental illness and the elderly.

Council members continue their extensive collaboration with other APA components and offices and with other medical organizations. The council has maintained a close working relationship with the Division of Government Relations and the National Institute of Mental Health.

Council members have provided invaluable advice and expertise regarding the complex federal laws and regulations pertaining to the care and treatment of the elderly in nursing homes and in regard to changes in the regulations governing the use of antipsychotic medications for the elderly. These comments prompted substantive changes in federal policy, particularly with respect to the provisions of the landmark nursing home reform legislation of 1987 on preadmission screening and resident review (PASARR) of the mentally ill in nursing homes.

Council members have served as a "quick response" resource for federal and state legislative and regulatory issues. Once the 1991 White House Conference on Aging is announced, the council and its Task Force on the White House Conference on Aging will act quickly to ensure that APA is well represented in the development of the conference agenda on issues pertaining to mental illness and the elderly.

Virtually all council components met during the 1990 fall meetings in Washington in September. The council received presentations from representatives of the Alzheimer's Association and AARP. AARP's representative presented to the council an outline of an ambitious proposal to establish a coalition of patient/consumer organizations and health care providers, including APA. The coalition's purpose would be to educate the public, federal and state lawmakers and staff, and health care professionals on issues pertaining to the care of the elderly mentally ill. The council unanimously endorsed the proposed coalition and recommended to the Board and to the Joint Reference Committee that APA formally join the coalition. The council also agreed to establish direct lines of communication with AARP and the Alzheimer's Association for discussing issues of mutual interest and concern.

The development of the coalition and the establishment of strong working relationships with beneficiary organizations, such as AARP, will help ensure that the council plays an important role in the coming decade in the formulation of policies on mental illness.

The *Task Force on Models of Care in Geropsychiatry,* Marion Goldstein, M.D., chairperson, is nearing completion of its report on the current status of the practice of geriatric psychiatry nationally and internationally. Emphasis will be on models of care that ensure continuity of care for the elderly and on caregivers and training sites that have done outcome studies which included evaluation of cost-effectiveness.

The *Task Force on the White House Conference on Aging,* Sanford Finkel, M.D., chairperson, is preparing its agenda for the 1991 White House Conference on Aging, which is expected to be held in late 1991. The task force expects to hold a meeting in December 1990 to establish a detailed agenda for the conference and will host two miniconferences on aging issues before the conference.

The *Committee on Long-Term Care and Treatment for the Elderly,* Ira Katz, M.D., chairperson, and the *Task Force on Reimbursement Options and Alternatives in the Psychiatric Care of Older Persons,* Howard Goldman, M.D., chairperson, met jointly in September 1990. Members of the committee and the task force continue to provide expert assistance to the Division of Government Relations on regulations pertaining to the treatment and care of the elderly in general and the elderly in nursing homes.

The committee was charged by the council to produce a new report on the appropriate use of antipsychotic medications for the elderly in nursing homes. The report will be published as an addendum to APA task force report 28, *Nursing Homes and the Mentally Ill Elderly* (1).

The *Corresponding Task Force on Geriatric Psychiatry in the Public Mental Health Sector,* Barry Fogel, M.D., chairperson, is nearing completion of a report tentatively titled "Geriatric Psychiatry and State Mental Health Systems."

The *Task Force on the Ethnic Minority Elderly,* Kenneth M. Sakauye, M.D., chairperson, is nearing completion of its survey of the literature on the problems of ethnic minority elderly and an annotated bibliography.

The *Task Force on Education and Training in Geriatric Psychiatry,* Charles Shamoian, M.D., chairperson, is also nearing completion of a resource document on training in geriatric psychiatry. The task force also met to discuss proposals on geriatric education put forward by the American Association for Geriatric Psychiatry.

REFERENCE

1. American Psychiatric Association Task Force Report 28: Nursing Homes and the Mentally Ill Elderly. Washington, DC, APA, 1989

The Council on Children, Adolescents, and Their Families

Lawrence A. Stone, Chairperson

The work of the council and its components continued to be directed toward maximizing APA's effectiveness in addressing the mental health needs of children, adolescents, and their families. This charge has been carried out through workshops, reports, position statements, and liaison with other APA components and allied organizations. The council has kept abreast of many issues that affect its patient populations through intramural and extramural liaison activities. Topics that have warranted considerable attention include practice guidelines, the *Report of the Secretary's Task Force on Youth Suicide* (1), the Institute of Medicine's report *Research on Children & Adolescents With Mental, Behavioral & Developmental Disorders: Mobilizing a National Initiative* (2), and the reported moves toward deinstitutionalization of children. The council recommended broad circulation of the entire report on youth suicide and underscored the importance of the inclusion of the section on suicide within the gay population. The council recommended APA's formal endorsement of the Institute of Medicine report and suggested that professional organizations and public advocacy groups give particular attention to fostering research training of child mental health professionals.

The APA Assembly of District Branches was advised of the council's concern about the deinstitutionalization of mentally ill children and of the request for referral of the issue to the Assembly Committee on Public Psychiatry and Task Force on Community Psychiatry for further study and possible action. The council expressed particular concern about the reported plans for deinstitutionalization because many of these children are from dysfunctional families.

Other liaison activities included 1) support of the plan of the Council on International Affairs to send an American delegation of child psychiatrists to Romania to aid institutionalized children, 2) review of the Act for Education of All Handicapped Children and recommendation that "serious emotional disturbance" be changed to "emotional and behavioral disorders" to allow more children to benefit from the provisions of Public Law 94-142, and 3) endorsement of an action paper, developed by the APA Task Force on Family/Systems Therapy, regarding preventive psychiatry during a national emergency. Recognizing that military families (and those who have family members stranded in Iraq and Kuwait) may need psychiatric services, the Task Force on Family/Systems Therapy advocated the development of a plan for providing services to those families at the district branch level.

A number of issues related to the severance of parental rights were reviewed, and the need for further study (by a new component) was discussed. The council voted to postpone recommending the establishment of a task force to study these issues until they could be further clarified.

The council received the report of the *Committee on Chronically Ill and Emotionally Handicapped Children,* Cynthia R. Pfeffer, M.D., chairperson. Emphasis was given to the need to involve child psychiatrists in negotiating changes in the provisions of Social Security Income/Social Security Disability Insurance. Critical issues involving this subject were discussed at this component's workshop, "Social Security Income/Social Security Disability Insurance Child Listings: Are They Appropriate?" at the 1990 annual meeting. For the next annual meeting, the committee proposed a workshop on stresses experienced by children and on children at risk for mental illness.

The *Committee on Family Violence and Sexual Abuse,* Sandra J. Kaplan, M.D., chairperson, is rewriting a position statement on child abuse and neglect, which should be completed by spring 1991. The committee is also drafting position statements on women and addiction and on babies born to mothers who use crack cocaine. The book "Family Violence: A Clinical Guide" is almost finished. Mr. Howard Davidson, a consultant from the American Bar Association, will write a segment on legal issues for each chapter. The council will review the document before publication.

The council requested rewriting of the position statement on capital punishment of minors drafted by the *Committee on Juvenile Justice Issues,* Richard C. Marohn, M.D., chairperson. The committee spent considerable time discussing decriminalization, truancy, violence in schools, and inappropriate hospitalization of adolescents. Recognizing the scarcity of empirical evidence concerning the inappropriate hospitalization of adolescents, the committee recommended the establishment of a task force to study the use and abuse of psychiatric hospitalization of minors. The council endorsed this recommendation. The committee completed the report "The Psychiatrist and the Juvenile Justice System," which was published in the *American Journal of Psychiatry* (3).

The *Work Group to Develop a Handbook for Psychiatric Practice Related to the Juvenile Justice System,* Michael G. Kalogerakis, M.D., chairperson, received a second grant from the Kenworthy-Swift Foundation to complete the handbook. The manuscript has been sent to the council for its review. The book advises psychiatrists on how to testify in juvenile court—what to do and what to avoid in order to be a credible witness.

Irving H. Berkovitz, M.D., chairperson of the *Committee on Psychiatry and Mental Health in the Schools,* has established a network of child and adolescent psychiatrists who spend a large portion of their time as consultants or service providers in schools. Of those who responded to Dr. Berkovitz's memo requesting information, 82% are child psychiatrists, 56% are primarily in private practice, and 12% work in academic settings. Of those who work in schools, 55% have had no formal training in this field; 20% work for free.

The council approved a position statement on school-based health clinics that the committee drafted. The statement urges APA to assist in increasing the number of psychiatrists participating in health clinics in elementary, middle, intermediate, and high schools.

The committee is also working on a monograph on psychiatric involvement in schools, which should be ready for the council's review in May 1991. It covers qualifications useful for psychiatrists consulting in schools, examples of psychiatric consultation, education of the handicapped, psychiatric involvement in educational programs for the handicapped, special experiences facilitating consultation, training considerations, and recommendations and prospects for the future. The council approved the committee's request to seek outside funding for the completion of this effort.

Myron Belfer, M.D., chairperson of the *Task Force on Day Care for Preschool Children,* has reviewed a considerable segment of the literature on day care. In preparation for the formal report, Dr. Aubrey Metcalf will review the issues that are specifically relevant to children and Dr. Moira Kennedy will study the issues pertaining to psychiatric residents and training.

The *Task Force on the Psychiatric Aspects of New Reproductive Technologies,* Miriam B. Rosenthal, M.D., chairperson, submitted an outline of its report to the council. The topics covered in the report will include the factors contributing to the psychological effects of infertility, the effects themselves, motivations for pregnancy, reproductive technologies, and psychological interventions.

Child and adolescent psychiatrists who attended the fall component meetings met to receive reports from representatives of several national organizations and individuals. The meeting was chaired by Dr. Lawrence A. Stone, who pointed out that the meeting provided an opportunity to highlight issues in particular geographical areas which warranted attention at the national, as well as local, level and that it served as a platform for sharing information of particular significance for the mental health of children, adolescents, and their families.

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3. The psychiatrist and the juvenile justice system (off acts). Am J Psychiatry 1990; 147:1584–1586

The Council on Economic Affairs

Robert Gibson, M.D., Chairperson

The activities of this council and its components during 1990 reflect APA's continued efforts to influence the many commercial and governmental entities that affect the provision of psychiatric care. Members of the council and components maintained liaison with representatives of such organizations as the Social Security Administration, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), the Health Care Financing Administration (HCFA), and major managed care and insurance companies.

When the Quality Assurance Committee was disbanded in May 1990, the Council on Economic Affairs asked Dr. Marlin Mattson, Dr. George Wilson, and Dr. Elaine Knutsen to complete the editing/revision of the *Manual of Psychiatric Quality Assurance.* The Council on Economic Affairs had an opportunity to suggest revisions to the document and concurred in recommending publication of the manual as a nonpolicy APA document. APA published the *Manual of Psychiatric Peer Review* in 1976 (1) and updated editions in 1981 (2) and 1985 (3). Because of the many changes in the field in recent years, a thorough revision has been attempted. It is hoped that the material, particularly the sections with criteria, will help our members.

The *Committee on Interprofessional Affairs,* William Webb, Jr., M.D., chairperson, continues its work with the Joint Commission on Interprofessional Affairs. The commission is made up of representatives from APA, the American Psychological Association, the National Association of Social Workers, and the American Nurses' Association. In 1990, the Joint Commission on Interprofessional Affairs obtained funding from the National Institute of Mental Health (NIMH), to be matched by the four sponsoring organizations, for a conference on interdisciplinary collaboration in 1991. The joint commission also has had preliminary discussions on areas of mutual interest related to the possible regulation of managed care organizations and the operational impact of the *CAPP v. Rank* decision.

Members of the *Committee on Hospital-Based or Hospital-Related Services,* Boris Astrachan, M.D., chairperson, were included in the Joint Task Force on the Survey of Psychiatric Hospitals, which was formed by the JCAHO to address problems with the current process for surveying psychiatric hospitals surveyed under the *Accreditation Manual for Hospitals.* As a short-term solution, the task force recommended that selected and modified standards drawn from the *Consolidated Standards Manual* be used in a tailored survey of hospitals by a single, specially trained survey team. The selected standards will address biopsychosocial rehabilitation, partial hospitalization, and residential services. As a long-term solution, the task force recommended that a task force on biopsychosocial rehabilitation be established by the end of 1990 to develop standards for both the *Accreditation Manual for Hospitals* and the *Consolidated Standards Manual.* Subsequently, standards for hospital-based partial hospitalization and rehabilitation services in the *Accreditation Manual for Hospitals* would be developed. It is planned that standards covering all three of the aforementioned services will be included in the *Accreditation Manual for Hospitals* by 1994.

The *Committee on Managed Care,* Steven Sharfstein, M.D., chairperson, became operational in 1990. The broad charge to the committee includes developing policy on provision of psychiatric care and the role of psychiatrists in managed care settings, conducting research, and developing and disseminating educational material. The committee also assumed responsibility for several projects begun by the Ad Hoc Committee on Managed Care Issues and developed a multifaceted response to issues in managed care, including a legislative and regulatory response, research, education, and a dialogue with the managed care industry. Its initial projects include 1) development of model state legislation for regulating utilization review companies, 2) an economic analysis of a national data base on costs for the treatment of mental illness and substance abuse, 3) establishment of a telephone service with an 800 number (800-343-4671) to ascertain, document, and address problems with managed care, 4) development of a managed care manual instructing members in the managed care process and facilitating access to services for psychiatric patients, 5) creation of a managed care network of district branch liaisons to disseminate information to and from the national district levels and work proactively on local issues, 6) initiation of a series of meetings and dialogue between the APA leadership and representatives of the managed care industry, and 7) establishment of a library of medical necessity criteria and standards used by the industry as they become available for professional review and commentary. The Ad Hoc Committee on Managed Care Issues continues oversight of the litigation feasibility study.

The *Task Force on Social Security Income/Social Security Disability Insurance,* Arthur T. Meyerson, M.D., chairperson, continues to communicate with the Social Security Administration concerning the listings for mental impairment for children. The child listings are in the form of proposed final regulations and are in the Office of Management and Budget. At the present time, the task force, which was involved in the development of the listings and commented on early versions, believes no action is appropriate. When the listings are published the task force will have an opportunity for comment again and will do so then if any substantial changes have been made. With regard to the decision in *Zebley v. Bowen,* which mandated an individual assessment of functional capacity for children, the regulation is being worked on by the Social Security Administration staff. An interim final regulation is in effect now, but there will be an opportunity for public comment on the new format. The task force will review and comment on the proposed final regulations at that time.

The task force is delighted about the addition of an expert in child psychiatry, Dr. Gail Edelson. It has submitted a proposal for a component workshop at the 1991 annual meeting that would be cosponsored by the Social Security Administration and the Academy of Child and Adolescent Psychiatry (and possibly the Council on Children, Adolescents, and Their Families). The subject would be the involvement of child psychiatrists in disability determination.

The *Work Group on the Harvard Resource-Based Relative Value Scale Study,* Donald Scherl, M.D., chairperson, continues to monitor federal proposals for paying physicians under Medicare. On Sept. 4, 1990, the HCFA published in the *Federal Register* a model resource-based relative value scale fee schedule (4). The HCFA has accepted comments on the model fee schedule, and APA has developed formal comments that address a number of psychiatry's concerns, including 1) the need for new and better codes in the *Current Procedural Terminology (CPT),* particularly new codes for visits and for evaluation and management, 2) the need for relative values that reflect differences in physician work due to variations in patients and sites of service, 3) the use of the fee schedule by nonphysician providers, and 4) questions about the impact of nonphysician use in the volume performance standard.

The *Work Group on Codes and Reimbursement,* Chester W. Schmidt, Jr., M.D., chairperson, continues to work with the American Medical Association on getting more appropriate codes for psychiatry included in future editions of *CPT.* The work group is also communicating with the HCFA about discrepancies with current billing protocols of Medicare carriers, identified through a survey conducted by the Office of Economic Affairs.

The *Task Force on Future Trends in Private Insurance,* Gary Tischler, M.D., chairperson, continued to explore issues related to managed care. The task force met with Steven Sharfstein, M.D., chairperson of the Committee on Managed Care, to discuss some of these issues, including educational programs for members, the variation in quality among utilization review firms, and problems concerning care of the chronically ill. The task force also reviewed *The Cleveland Admission, Discharge and Transfer Criteria: Model for Chemical Dependency Treatment Programs* (5) and voted to recommend the criteria as a useful model for examining one group of psychiatric illnesses.

The *Committee on Financing and Marketing,* Robert O. Friedel, M.D., chairperson, has focused on marketing assistance for APA members, primarily through the district branches. Its major concerns include negative trends in corporate response, decreasing insurance benefits for psychiatric care, inappropriate and appropriate utilization management activities, and a blurring of the roles of psychiatrists and psychologists. The committee set and accomplished the following goals for the year: 1) sending a questionnaire to all APA members who received the marketing manual (produced last year by the committee in conjunction with the Office of Economic Affairs) to determine what additional information should be included, 2) assisting the district branches in their marketing efforts, 3) preparing a series of information materials for a larger group of APA members, and 4) sponsoring and presenting a workshop at the 1990 annual meeting.

The *Committee on Occupational Psychiatry,* Peter L. Brill, M.D., chairperson, has continued to address mental health in the workplace. The committee has sponsored several events at annual meetings. The focus of the committee is on work stress and psychopathology at work. Current projects of the committee are 1) preparing an article on the history of occupational psychiatry, 2) writing a policy statement on the insufficient recognition of the effect of workplace stress on family life, 3) developing a paper on stress as related to workmen's compensation insurance, and 4) writing a policy statement on work histories (contribution of work to the employee's present problem and treatment options).

The *Task Force on Psychiatrist Payment,* Boris Astrachan, M.D., chairperson, was established to examine the nature of psychiatrists' income, including the diversity of practice settings, sources of reimbursement, costs associated with various types of practice, the impact of public and private coverage, and the ramifications of changes in health care organizations. The task force is analyzing economic information from the APA membership survey and will issue detailed reports on practice settings, income, sources of payment, and patient characteristics of psychiatrists. The task force will complete its work in 1991.

The *Task Force on Prospective Payment Issues,* Joseph T. English, M.D., chairperson, continued to monitor payment issues and to explore potential alternative payment mechanisms. Among these efforts was a review of studies by NIMH of federal legislative and administrative activities related to prospective payment for psychiatry. The task force believes there are no immediate threats to psychiatry's exempt status within the prospective payment system but cautioned the council about an emerging perception in the field that the recent increase in psychiatric facilities may be related to the exempt status. The task force is monitoring several innovative payment reform initiatives under way in the states. These are being watched closely by the federal government and the field.

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4. Federal Register 1990; 55(171):36178
5. Greater Cleveland Hospital Association: The Cleveland Admission, Discharge and Transfer Criteria: Model for Chemical Dependency Treatment Programs. Cleveland, Greater Cleveland Hospital Association, 1990

The Council on Internal Organization

Bernice B. Elkin, M.D., Chairperson

The council oversees "all those matters involved in the organizational structure of the Association not covered by constitutional committees." There are 11 components that report directly to the council and 16 components that report to committees under the council, primarily award boards and subcommittees of the Scientific Program Committee. The council thus has responsibility for a wide range of activities: maintenance of the APA headquarters; benefits offered to members, such as the legal consultation plan; program content, exhibits, and arrangements for the annual meetings; advertising policy; data processing, telecommunications, and other information systems within the Association; various prizes and awards given by APA in recognition of outstanding achievement; personnel and staff benefit programs; and the federation of auxiliary organizations. Following are the highlights of council and component activities over the past year.

The *Committee on Advertisers and Exhibitors,* Henry H. Work, M.D., chairperson, is composed of representatives from the Council on Internal Organization, the Council on Medical Education and Career Development, the Institute on Hospital & Community Psychiatry Program Committee, and the Scientific Program Committee.

For the last 2 years, a reception sponsored by the APA exhibitors at the annual meeting has been held in the exhibit area on Monday evening. It has not been very successful, so it will no longer be held.

The *Daily Bulletin,* published during APA's annual meetings, was published in house this year. The shift to in-house publication was extremely successful, and the committee anticipates publishing the bulletin in the same manner next year.

The *Committee on Advertising,* William D. Strathmann, M.D., chairperson, serves as an advisory board to APA's three major periodicals (*Psychiatric News, American Journal of Psychiatry,* and *Hospital & Community Psychiatry*) regarding questionable advertisements either submitted for publication or being considered for solicitation for publication. The committee works closely with the Committee on Advertisers and Exhibitors to keep the latter informed about advertisements it recommends for rejection.

The editors of the three periodicals are currently reviewing APA's principles and guidelines for advertisements and may recommend small revisions because of the increase in advertising for medical equipment, psychiatric facilities, and dietary supplements. Any revisions will be presented to the council in September 1991.

Fred Gottlieb, M.D., chairperson of the *Committee on Friends of the APA,* stated that the Lifers Group, made up of Life Members, Life Fellows, and Life Associates and led by Dr. Harold Berson, is considering joining the umbrella organization, the Federation of Friends of the APA. The committee is planning to contact the Gay/Lesbian Caucus and the Committee on Women regarding forming additional groups under the federation, such as groups for nonspouse partners and for husbands.

The *Committee on Grants and Awards,* Mary Jane England, M.D., chairperson, considered several awards this year: a human rights award, a "lifers" award, and an award from the Masserman Foundation for International Accord. None of these has yet been approved.

The committee discussed a proposal to change the policy of not naming an award for a living person. The committee is exploring the advantages and disadvantages of this policy.

In June 1990 the Board of Trustees discussed concerns about the process for determining recipients of APA's awards. Two Board actions resulted from this discussion: 1) a request that the council present to the Board in September 1990 a list of award winners who will be asked to present lectures during the next annual meeting and 2) a request that the council reorganize the awards process to ensure adequate oversight of awards components. The committee is still refining a reorganization plan.

The *Committee on History and Library,* Martha J. Kirkpatrick, M.D., chairperson, is developing a program for the 1991 annual meeting. The activities being considered include an exhibit of the Freud antiques and an exhibit of photographs of state hospitals and other subjects. The council approved the committee's contacting the editor of the *American Journal of Psychiatry* concerning the possibility of a special issue of the *Journal* containing landmark articles, each published along with contemporary commentary.

The *Committee on Information Systems,* Zebulon C. Taintor, chairperson, is working with staff to develop a telephone service by which members will be able to listen to messages on topics of interest that are read by a computer-generated voice. The caller will be asked to press particular buttons on his or her telephone to be connected with messages on a specific topic. The subjects planned for this service so far are government relations, the annual meeting, and the project involving collaboration between academic departments of psychiatry and state departments of mental health.

The committee is also looking into the possibility of an informal newsletter to promote communication among APA members who are interested in using computers in psychiatry. This project is still under development.

The committee is considering two programs for the 1991 annual meeting: a component workshop and a software presentation.

The *Committee on Special Benefit Programs,* Eva B. Ebin, M.D., chairperson, discussed several new APA member benefits. A proposal from Meridian One Corporation to offer members discounts for office equipment, Sprint long-distance telephone service, and Alamo car rental was approved by the council. A new retirement program, originally designed to offer members financial planning, has been restructured as a retirement planning program.

The committee is looking into other possible programs, such as a portable telephone service and discount AT&T long-distance telephone service.

Jane H. Preston, M.D., chairperson of the *Committee on Telemedical Services,* has kept the council up to date on the rapidly changing field of telemedicine. The committee is working toward establishment of an American Medical Association telemedicine committee and toward inclusion of a psychiatrist on that committee.

The committee is also addressing 1) the use of interactive video for outreach to rural areas without medical services and 2) reimbursement problems that occur when the doctor and the patient are in different locations. At this time, the Health Care Financing Administration will not provide reimbursement for treatment when the doctor and the patient are in different rooms. Also at issue is reimbursement for transmission costs.

The committee has requested permission to seek outside funding to support a scientific exhibit at the 1992 annual meeting.

The *Headquarters Committee,* Raymond I. Band, M.D., chairperson, is charged with oversight of the APA headquarters building. When APA terminated the quality assurance program, 16,000 square feet of office space became empty. Space has now been subleased by the Administrative Office of the U.S. Courts.

Also discussed was the role of this committee in regard to being informed about or providing input into the management of the APA building. The council suggested that the committee review its charge and discuss the issue during the annual meeting.

The *Personnel Committee,* Maurice J. Martin, M.D., chairperson, is reviewing the policy on temporary and casual employees. A proposed change would require approval from the Deputy Medical Director for temporary employees to work beyond 6 months. The committee is developing policies regarding sexual harassment, drugs in the workplace, absenteeism, and smoking.

The cost of the health insurance plan for employees was about to rise sharply because of a 40% drop in participation caused by the loss of the employees in the Office of Quality Assurance. The Association changed plans as of Nov. 1, 1990.

The *Scientific Program Committee,* Allan Tasman, M.D., chairperson, reported that the 1990 annual meeting in New York was attended by nearly 16,000 people and broke all previous records for total attendance, attendance by APA members, and attendance by Members-in-Training. In response to members' wishes, there were more research activities and more small-group interactive sessions than in previous years. A new format, the round-table discussion, was instituted in 1990, and forums were revived after a long absence.

In September 1989 the Board of Trustees approved the council's recommendation that $10,000 be allocated for a trial program to provide sign-language interpreters for hearing-impaired APA members during the 1990 annual meeting. The Office to Coordinate the Annual Meeting received one request for these services for the 1990 meeting. Although the need among our members may be small, the council felt it would be in the best interest of the Association to have funds available for this purpose. Therefore, the council presented to the Board in September a recommendation that $3,000 be included in the 1991 annual meeting budget to enable APA to provide these services if requested. This recommendation was approved by the Board.

For the 1991 meeting, the committee anticipates only minor modification of the session formats, but the noon forums will be reinstituted. They will provide an opportunity for sessions that do not fit into the usual formats.

The Joint Reference Committee had raised questions concerning the industry-sponsored symposia and general pharmaceutical support of the annual meeting. These symposia are reviewed by Dr. Tasman and Dr. Henry Work, chairperson of the Committee on Advertisers and Exhibitors. While Dr. Tasman is aware of the concerns being raised, overall he is confident that the symposia provide excellent educational opportunities for our members. He also noted that the income generated from these sessions helps to support other activities during the meeting. The committee plans to meet with industry representatives next May to develop better communication. APA guidelines for the symposia are under review and will be revised if necessary.

Also discussed was the size of the committee: presently it consists of 16 members, five consultants, and one Burroughs Wellcome Fellow. The number of members has not changed in several years, but the workload has expanded significantly. The council recommended to the Joint Reference Committee in September that the Board consider increasing the size of this committee.

The council felt that some components may need to have their charges updated or clarified. Council members will review these charges before the next meeting. At that time the council will discuss possible modifications.

In summary, the Council on Internal Organization continues to represent APA members in the business and internal workings of the Association. It welcomes all input and comments from members.

The Council on International Affairs

Paul J. Fink, M.D., Chairperson

The Council on International Affairs is the membership component that oversees APA's international activities and makes policy recommendations to the APA Board of Trustees related to activities international in scope. It deals with all questions pertaining to psychiatry and international relations that are presented by APA members, other components, and staff.

The council has initiated a number of important APA projects during this past year, which has seen many political changes around the world. The council was given permission by the APA Board of Trustees to seek outside funding for a very exciting project related to Eastern European psychiatry. An open meeting was held during the 1990 APA annual meeting to discuss how the APA membership might meet the growing needs of psychiatrists and their patients in Eastern Europe and the Soviet Union. The council was gratified by the response from the participants in this meeting and is now formulating a project whereby a team of American experts in specific areas of psychiatry would travel to Eastern Europe to give lectures and hold seminars on specific aspects of American psychiatry. These Americans would, in turn, learn about psychiatry in the host countries and hold round-table discussions to plan future activities and collaboration. It is hoped that these visits will occur in the fall of 1991. The council would like to express its appreciation to the many APA members who have contributed books and journals to psychiatrists in Eastern Europe, through the APA Office of International Affairs. We have heard that these contributions have already provided valuable resources to psychiatrists in these countries who have not had the benefit of international publications.

For many years APA has organized joint scientific meetings with other countries, approximately once every 2 years. We have had meetings in a number of countries, including France, Ireland, Kenya, China, and, most recently, Germany; the meeting in Germany will be mentioned later in this report. The organization of these meetings has considerably increased the responsibility of the staff of the Office of International Affairs at a time of diminishing financial resources in APA. Thus, the council has recommended that unless additional staff is allocated for the Office of International Affairs APA cease the organization of these meetings in other countries. The meeting planned for Barbados in May 1991 will be the last joint meeting organized by APA. The council and staff will be formulating ways to enhance participation by APA members in other worthwhile international meetings but will not organize these meetings directly.

The council was very pleased with the outcome of the joint meeting in Germany, Oct. 1–7, 1991, which began with a satellite symposium in Mainz, another in Mannheim/Heidelberg, another in Munich, and the main plenary session in Bad Kissingen. The satellite symposia, which provided an excellent orientation to German psychiatry, were organized by Professor Otto Benkert of the University of Mainz, Professor H. Hafner of the Central Institute of Mental Health in Mannheim, and Professor H. Hippius at the University of Munich. The plenary meeting in Bad Kissingen, opened by Dr. Johannes Meyer-Lindenberg, President of the German Society of Psychiatry and Nervous Diseases, and Dr. Elissa Benedek, President of APA, focused on child psychiatry, classification, new psychotropic drugs, genetics, eating disorders, brain imaging, émigrés and persecution, and the effects of economics and politics on psychiatry.

The joint meeting in Barbados, May 17–20, 1991, will immediately follow the APA annual meeting in New Orleans. The topics to be covered at this meeting are geriatrics, substance abuse, forensic psychiatry, mental health service delivery, and the psychiatric sequelae of natural disasters. This should be a most interesting and pleasant ending to the annual meeting, and we urge interested APA members to contact the Office of International Affairs for more information.

The council is pleased with the APA decision to participate in the American Association for the Advancement of Science's program to distribute journals in sub-Saharan Africa and hopes that this program will continue.

The council continues to be involved in the excellent International Scholars Program at the APA annual meetings and appreciates the efforts of the Scientific Program Committee in this regard. The council has organized a component workshop for presentation at the APA annual meeting in New Orleans in the hope of educating our membership on the many worthwhile APA activities in the international arena. It is hoped that many APA members will participate in this workshop.

The *Committee on International Education*, Normund Wong, M.D., chairperson, has reviewed the first applications by psychiatrists to the International Medical Scholars Program, which is administered by the Educational Commission on Foreign Medical Graduates. The committee is proud to provide the psychiatric component in this important project, which brings certified midcareer psychiatrists from other countries to the United States to study specific areas of our profession for 3 months to 3 years. The committee will facilitate placement of applicants who are approved for the program and will monitor their progress. The committee is also considering publication of a booklet on psychiatry in other countries. The data for the booklet would be obtained from the research and networks already established by the Office of International Affairs. The committee was pleased to learn that this office has close contacts with psychiatrists and those responsible for mental health policy in over 90 countries. This network is often used by APA members for patient referrals and contacts for possible scientific collaboration, but the committee believes that the material needs to be made available in printed form to facilitate these activities among our members. The committee will also hold a component workshop during the APA annual meeting in New Orleans, and special invitations will be sent to training directors in the United States and to all international visitors attending the meeting.

The *Committee on Abuse and Misuse of Psychiatry and Psychiatrists,* Joseph Bloom, M.D., chairperson, has continued to make the APA leadership aware of psychiatric abuse issues in all countries. The committee has followed the progress of the World Psychiatric Association (WPA) in its efforts to enforce the conditions placed on the All Union Society of Psychiatrists and Narcologists of the U.S.S.R. before it was readmitted to the WPA and has supported the Independent Psychiatric Associations that have been formed in the Soviet Union. At the same time, the committee believes there is still much work to be done on these issues and has recommended the following position for APA:

> The American Psychiatric Association continues to follow developments in Soviet psychiatry. It welcomes recent changes. However, since the completion of the U.S. delegation's visit to the Soviet Union in February 1989, areas of significant concern remain. In light of these concerns, APA should encourage:
>
> 1. Reform in the leadership of Soviet psychiatry.
> 2. Public acknowledgment of past psychiatric abuse by the Soviet government.
> 3. Improvement in Soviet mental health law.
> 4. Discontinuation of abuses associated with the psychiatric Registry.
> 5. Rehabilitation and compensation for victims of psychiatric abuse and their families.
> 6. Establishment of a functioning psychiatric ethics panel within the All Union Society of Psychiatrists and Narcologists (AUSPN).
> 7. Collaboration with the newly emerging Independent Psychiatric Association (IPA).

Further, the committee has suggested,

> The APA should identify and give major support to those psychiatrists who have demonstrated an ethical posture in those countries where systematic psychiatric abuse has occurred. These psychiatrists should be invited to APA programs, courses, meetings. And there should be an active program of having such psychiatrists invited, through APA involvement, to courses, institutes, etc., of other psychiatric organizations and departments. In addition to using its own funds, the APA should actively seek foundation grants and other funds for such ventures. It is the APA's belief that this approach will support such psychiatrists' movement toward positions of leadership, thus aiding in the elimination of psychiatric abuse in their respective countries.

The *Committee on Human Rights,* Loren Roth, M.D., chairperson, has addressed a number of vital issues this past year. First, as authorized by the APA Board of Trustees, it began collaborating with appropriate government agencies to address the mental health needs of the American hostages in the Middle East and their families. APA leaders have been in contact with government officials working on this problem and are coordinating efforts by the district branches to assist in this effort.

The committee is also establishing an "urgent action" network among APA members. The committee is working with the district branches on this project. In addition, it is preparing a booklet on psychiatry and human rights, which the committee hopes will be published by APA. This booklet is the beginning of the educational efforts planned by the committee. Another is a half-day symposium on human rights and psychiatry for the APA annual meeting in 1992 in Washington, D.C. The committee continues to urge the APA leadership to establish a human rights award or prized lectureship in the APA structure whereby individuals and organizations that have been active in the human rights arena could be honored. In addition, there is great concern about the plight of institutionalized children in Romania, and the committee is looking into ways APA can help with this tragic situation. Another important project suggested by this committee is the cosponsorship with the American Association for the Advancement of Science and other organizations of a conference on the physical and mental trauma children experience as a result of human rights violations.

The Committee on Human Rights has been gratified by the communications from APA members on a wide variety of important human rights problems. However, occasionally it has had to make the difficult decision that a certain issue is not in the scope of this committee. It was particularly interesting that a number of APA members signed a petition asking the committee to address the Turkish genocide of Armenians. Although the committee greatly sympathizes with the concerns of these members, it believes that such a project is outside the scope of its charge.

The *Task Force on Conflict Resolution,* Curtis Bristol, M.D., chairperson, has received permission from the Board of Trustees to seek outside funding of its upcoming academic study of conflict resolution. Dr. Bristol intends to put together an interdisciplinary study group to address such issues as boundary function, resolution of aggression, and dynamics, rather than limiting the work to seeking practical applications.

The *Task Force on APA Liaison With the WPA,* Eugene Feigelson, M.D., chairperson, is studying the activities of the WPA and will be making recommendations to the APA leadership as to how we might better collaborate with the WPA and support its ongoing work. We are pleased to have two Americans on the Executive Committee of the WPA, but the council is eager to have a monitoring function within the WPA's council structure so that it can have more input into WPA activities.

The council is studying the problems of mental health care delivery in countries with very limited economic resources. However, there are a number of reports of extremely substandard care in countries that are more economically developed. One such example is the deplorable treatment of psychiatric patients on the island of Leros, Greece. The council therefore asked APA to send an official complaint to the WPA about the psychiatric situation on Leros.

The council is also working on ways to increase the international membership of APA and is awaiting a report from the Committee on Membership as to how we might accomplish this goal.

In summary, the council welcomes all suggestions from APA members regarding its international activities and looks forward to discussing these issues with members throughout the year.

The Council on Medical Education and Career Development

Jerald Kay, M.D., Chairperson

The council's area of responsibility is the entire spectrum of medical education, for both psychiatrists and, where appropriate, other physicians. Its responsibilities include fostering the education and the professionalization of medical students, residents, and practitioners. The council is also involved with subspecialties and special areas of clinical interest, such as child and adolescent psychiatry, consultation-liaison psychiatry, and administrative psychiatry. The council and its 18 components are active in recruiting medical students into psychiatry and in enhancing the career development of psychiatrists in all phases of their practice. In addition, it also has primary responsibility for implementing and monitoring the APA continuing medical education (CME) requirement for members, which promotes the highest quality of psychiatric care and encourages the continuing professional growth of psychiatrists. Many of the activities of the council involve liaisons with other associations, accrediting and certifying bodies, and other organizations.

The *Committee on Administrative Psychiatry,* Stephen Rachlin, M.D., chairperson, reported the results of the administrative psychiatry oral examination, which was held on May 12, 1990. Of the 13 individuals examined, six passed and have been certified by the committee, four conditioned, and three failed. The committee announced that Jack F. Wilder, M.D., has been named as the recipient of the 1991 Administrative Psychiatry Award.

The *Committee on Consultation-Liaison Psychiatry and Primary Care Education,* Thomas N. Wise, M.D., chairperson, reported on its development of a policy statement on psychiatric education of primary care physicians. This proposed policy statement was prepared in response to offers from pharmaceutical companies to assist APA in developing educational materials for primary care physicians.

The *Committee on Continuing Education,* Pauline Langsley, M.D., chairperson, completed its report, "Continuing Education for Psychiatrists: A Contemporary Definition," which was accepted by the council in September 1990. The council also approved distribution of a questionnaire to all APA components requesting information on upcoming CME activities, in an effort to compile a complete listing for dissemination to the APA membership.

The committee also reported on issues to be considered in 1991, including the revision of the American Medical Association CME requirement, development of an annual guide to recently published literature affecting clinical practice, and possible assessment of members' educational needs, especially with respect to recertification.

The *Committee on Graduate Education,* Sherwyn M. Woods, M.D., chairperson, reported on the importance of collecting model curricula and audiovisual teaching materials and disseminating them to residency training programs. The committee will work with the Office of Education to implement this project. The committee reviewed the "Report of the APA Task Force on Prevention Research" (1) and suggested consideration of developing an appropriate curriculum on prevention for presentation to the Curriculum Committee of the American Association of Directors of Psychiatric Residency Training and a workshop presentation at its annual meeting in 1991.

The committee reviewed a communication to the field by the Accreditation Council for Graduate Medical Education regarding professional standards review organizations' assignment of points to residents. The committee felt that the assignment of points was inappropriate and will work through the proper APA channels to communicate its concern to the Accreditation Council for Graduate Medical Education.

The committee reviewed the current proposals from the American Board of Psychiatry and Neurology (ABPN) and the Residency Review Committee for Psychiatry regarding methods for documenting a resident's progress through general and child training programs and for verifying successful completion of a resident's training. It reaffirmed its previous statement on the need to preserve educational integrity by using some form of documentation of residents' clinical experiences, but it decided to reexamine this issue once the draft guidelines have been received.

The *Committee on the Impaired Physician,* Malkah T. Notman, M.D., chairperson, completed its work on "Guidelines to District Branches for a Policy on Physician Impairment." These guidelines have been developed to assist district branch committees on impaired physicians to function more effectively and efficiently in early recognition, evaluation, referral, treatment, and reentry into practice for impaired psychiatrists. The council recommended to the Joint Reference Committee, the Assembly, and the Board of Trustees that the guidelines be approved and distributed to impaired physicians committees in the district branches.

After a review by the Committee on Graduate Education and the Committee of Residents and Fellows, the proposed "Guidelines for Mental Health Services for Medical Students and Residents" was presented to the council in September 1990. The council recommended that this document receive additional editing and sent it back to the committee for reworking and eventual distribution to the American Association of Directors of Psychiatric Residency Training, the Association of Directors of Medical Student Education Programs, deans of student affairs, directors of student health centers, APA district branches, the AMA Physician Health Committee, and other related organizations.

The *Committee on Medical Student Education,* Leah J. Dickstein, M.D., chairperson, reported on the need to continue to recruit medical students into psychiatry and to update the recruitment materials targeted for medical students. The council approved the committee's request to seek outside funds to pay for upgrading the "Careers in Psychiatry" photograph display and completing the recruitment videotape, which will be used at the annual conventions of the American Medical Student Association and the Student National Medical Association. The committee will continue to send representatives to these meetings, which have proven to be important vehicles for recruitment.

The committee completed its work on the Nancy C.A. Roeske Award Certificate for Excellence in Medical Student Education. The first certificates will be presented during the 1991 APA annual meeting, in New Orleans.

The committee discussed the results of the 1990 National Residency Matching Plan and its implications for psychiatry and agreed that recruiting more medical students into psychiatry should be made a priority by the field. With this in mind, the committee sought and received approval to publish a 1-page self-mailing medical student newsletter titled "Lucid Associations," which will be distributed to all Medical Student Members of APA and medical school psychiatry clubs.

The second Medical Student Day luncheon was held during the 1990 annual meeting and was a great success. Over 300 medical students, residents, psychiatry residency training directors, and distinguished leaders in psychiatry attended. As long as outside funding is available, the committee will continue to sponsor the luncheon to encourage medical students to attend the annual meeting and to enter psychiatry.

The *Committee on Psychiatrist Leadership in Public Mental Health Programs,* Robert Leon, M.D., chairperson, fulfilled its charge and was therefore disbanded in May 1990. The committee was thanked for its work and its contribution to the field of psychiatry. The committee's paper "Leadership in Public Mental Health Facilities: Guidelines for the Chief Executive Officer and the Medical/Clinical Director" was approved by the Board of Trustees and is now official APA policy.

The *Committee of Residents and Fellows,* Elisa Triffleman, M.D., chairperson, reported on the committee's concern regarding the need to increase dues gradually for Members-in-Training as they advance to General Member and to enhance the retention of Members-in-Training as General Members of the Association. It was reported that 8% of General Members are former Members-in-Training. The committee will examine further this issue and explore ways to help district branches retain Young Psychiatrists in APA (a Young Psychiatrist is a psychiatrist who is younger than 40 years or has practiced less than 5 years).

The committee discussed the feasibility of lobbying on Capitol Hill during its two meetings each year in Washington, D.C. It is especially concerned with issues that relate to residents and their training (e.g., managed care, restoring the deductibility of interest on student loans). The committee will work with the Division of Government Relations to plan and coordinate this effort.

The committee, along with the other resident and fellowship components, continues to address ways to bring Members-in-Training and Young Psychiatrists into the mainstream of the Association at the national and district branch levels once their terms on resident/fellowship components have ended.

The *Steering Committee, Psychiatric Knowledge and Skills Self-Assessment Program VI (PKSAP VI),* Gordon Strauss, M.D., chairperson, reported that module C of PKSAP VI was mailed to subscribers in May 1990, and the deadline for comparison scoring was Aug. 31. With the purchase of scanning equipment, the staff in the Office of Education now have the capability and responsibility for scoring the PKSAP VI answer sheets. This self-assessment program is offered on a continuous basis.

The *Task Force on Educational Activities for Diagnostic Systems,* Michael Fauman, M.D., chairperson, reported that the diagnostic practice survey, on the use of *DSM-III-R,* has been mailed to practitioners. The task force will, in addition, compile a listing of all existing *DSM-III-R* teaching tools, which can be sent to members on request.

The *Task Force to Facilitate Communication Between the APA and ABPN,* Richard Shader, M.D., chairperson, reported on the need to better publicize the process by which ABPN directors are nominated. Many had expressed concern that the nomination process has not been fair to all persons interested in being considered; the Ad Hoc Committee to Develop a Slate of Candidates for Election to the ABPN has experienced political lobbying for some candidates and does not consider such efforts appropriate. If letters to APA members and articles in *Psychiatric News* were used to advertise the process, the cost would be minimal. Further, the task force reported that the dates of the ABPN part II examinations, the locations of the examinations, and the process used to select examiners should be widely publicized.

The *Task Force on Post Residency Fellowship Programs,* George Pollock, M.D., chairperson, was granted a 2-year extension to complete its descriptive list of fellowship programs, which will be used as an appendix to the *Directory of Psychiatry Residency Training Programs,* and its recommendations for an APA policy on recognition and accreditation of fellowship programs. The task force will also collaborate with the Commission on Subspecialization on the policy effort.

The *Task Force on Recertification,* Joe Tupin, M.D., chairperson, recommended that APA develop regional and local CME programs through a consortium arrangement with the district branches and area councils for members interested in becoming Board certified. The task force has completed its charge to study existing and proposed recertification activities of other medical specialty organizations and has developed recommendations for recertification programs in psychiatry. It has submitted its final report, which includes the recommendation that the task force be disbanded. It recommended that a permanent standing component of the Association be established to work with representatives of the ABPN to develop an educational program to assist members in preparing for recertification and, for members who are currently in practice but are not Board certified, initial certification. The results of the survey of approximately 1,000 non-Board-certified APA members (40% response rate) revealed that approximately one-half are interested in becoming Board certified. By extrapolation, the task force estimates that between 3,500 and 4,500 non-Board-certified members of APA are interested in obtaining Board certification. Further, it discovered that these practitioners' primary motivation for seeking certification is lower-cost liability insurance. Moreover, the respondents reported that home study methods (such as PKSAP and the annual review update) were most attractive.

The *Committee of Young Psychiatrists,* David Whitehouse, M.D., chairperson, reported on the success of the process for choosing the recipient of the first APA/Wisniewski Young Psychiatrist Research Award. The award board received over 36 papers. The recipient, Eric Hollander, M.D., was awarded an honorarium of $2,000 and the two psychiatrists who received honorable mentions received $500 each.

The committee, along with the Committee of Residents and Fellows and other resident groups, is concerned about retention of Members-in-Training and Young Psychiatrists as they advance to General Membership in the Association. It will work with the Committee on Membership to study this issue. Additionally, the committee is preparing a study to identify young psychiatrists and collect data on their practice patterns, their professional concerns, and the impact of the transition from residency into practice.

The *Work Group on Disclosure of Confidential Personal Information,* Malkah T. Notman, M.D., chairperson, presented a draft document titled "Guidelines Concerning Disclosures and Confidentiality" to the council in September 1990. The council provided recommendations for revising the document, which included greater specificity in defining psychiatric illness and hospitalization, so that regulatory boards would consider the policy statement more seriously. The council will review this document during its May 1991 meeting.

The *APA/Mead Johnson Fellowship Selection Committee,* James Barter, M.D., chairperson, reported that the 1990–1991 APA/Mead Johnson Fellows were selected during the June 1990 meeting and there were no major discrepancies in the ranking among the members of the selection committee. After the selections were made, it was agreed that the selection process should remain substantially as is.

The committee reviewed and accepted the guidelines for presentations by APA/Mead Johnson Fellows at the H&CP Institute, which were drafted by Dr. Barter, and felt that adoption of the guidelines would expedite program participation.

The *Selection/Advisory Committee of the APA/NIMH Minority Fellowship Program,* Charles Pinderhughes, M.D., chairperson, reported that of the 18 residents who applied for the 1990–1991 fellowship program, seven were selected. In addition, the committee selected four alternates and named five 1989–1990 fellows as trainee consultants.

The committee sought approval to publish the proceedings of the 1986 fellows' symposium "Ethnic Difference: Do You Amend Your Therapeutic Approach" as a monograph.

The *APA/Burroughs Wellcome Fellowship Selection and Program Committee,* Roger Peele, M.D., chairperson, reported that of 44 nominees, 10 fellows were selected for 1990–1991.

REFERENCE

1. Report of the APA Task Force on Prevention Research (off acts). Am J Psychiatry 1990; 147:1701–1704

The Council on National Affairs

Lindbergh S. Sata, M.D., Chairperson

This council is responsible for matters of national interest to psychiatry and the patients it serves. Social and health-related issues that affect underrepresented groups in the general population and within the profession warrant particular attention by this council. To tackle these issues, the council works closely with representatives from the Assembly, APA staff, and relevant APA components while overseeing and assisting the 11 components under its aegis.

The usual connotation of "prevention" is primary prevention, and the council concerns itself with other types of prevention. To make this clear and to reiterate its interest in all aspects of psychiatric practice, the council voted to revise part of its charge to read, "The multiple approaches appropriate to such *issues* include an emphasis on *clinical care, research, service delivery and systems of care, and primary, secondary, and tertiary* prevention" (italics indicate changes).

The council has taken steps to bring together its components by convening a meeting of component chairpersons during the fall meetings to enable them to exchange ideas, consolidate efforts, and unite behind certain positions and recommendations.

The *Committee on Abuse and Misuse of Psychiatry in the U.S.,* Jose M. Pena, M.D., chairperson, is revising its white paper "Abuse and Misuse of Psychiatry in the U.S.: The Need for an Institutional Ethics." The committee will resubmit it to the Council on National Affairs for a second review before requesting permission to publish it. Meanwhile the committee is trying to gather information about psychiatric care in federal prisons in an effort to determine the role of psychiatry and psychiatrists in the federal prison system. The committee reviewed the court decision in *Baraldini et al. v. Meese et al.* (1). While the case does not involve abuse of psychiatry, the committee feels there are psychological sequelae in this and similar cases because of the prison environment itself and the treatment of prisoners. The committee also wants to find out if and how mental health and correctional staff functions are kept separate.

Thus far the committee has responded to requests for help and to allegations of abuse and misuse of psychiatry in the United States. It now has decided to act rather than just react and will study psychiatrists' role in the treatment of AIDS. There are no complaints about this role thus far, but the committee considers this part of the treatment of AIDs very important. It will also work with the Council on Children, Adolescents, and Their Families to examine the possibility of abuse in cases of involuntary hospitalization of adolescents.

At the 1991 annual meeting the committee plans to meet with the National Alliance for the Mentally Ill and other patient groups to consider working together on a data base of alleged cases of abuse and misuse put forward by patients.

The *Committee of American Indian/Alaskan Native Psychiatrists,* David Foos, M.D., chairperson, discussed prescription privileges for psychologists in the Indian Health Service (IHS). Part of the problem is the reluctance of physicians in the IHS to treat the mentally ill because they feel they do not have the time or the expertise. The committee suggested that these physicians be trained in psychiatric issues and that the IHS recruit psychiatrists.

The committee will work on a proposal for a curriculum on American Indian and Alaska Native issues and culture with the help of staff at the National Center for American Indian and Alaska Native Mental Health Research.

The *Committee of Asian-American Psychiatrists,* Francis G. Lu, M.D., chairperson, wants to recruit Asian-American medical students for psychiatry and Asian-American psychiatrists for APA and to help keep them in APA. To accomplish the first, the committee will work with the APA/NIMH Fellows, who will compile a directory of minority psychiatry residents. The committee will talk with the chairpersons of the Committee on Membership and the Assembly Committee on Recruitment and Participation before starting on this task.

Like the council and its other components, this committee reviewed its charge and, to emphasize its recruitment efforts, decided to add the following: "encourages membership and involvement of Asian-American psychiatrists in the American Psychiatric Association."

The U.S. Department of Health and Human Services' *Guidelines for Supplements for Underrepresented Minorities in Biomedical and Behavioral Research Supported by ADAMHA* (2) says, "In awarding supplements, ADAMHA will give priority to projects involving Blacks, Hispanics, Native Americans, Pacific Islanders or other ethnic or racial group members who have been found to be underrepresented in biomedical or behavioral research nationally." Asian-Americans are conspicuously absent from this list. The committee questions the implication that Asian-Americans are not an underrepresented minority in biomedical and behavioral research. The committee drafted a letter voicing its concern to Dr. Frederick K. Goodwin, administrator of the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA).

Like the other minority committees of the council, the Committee of Asian-American Psychiatrists discussed the reduction of mental health services, the cut in research and training funds, the stigma of mental illness, and racially motivated violence. This committee is working with the other minority committees on these issues.

The committee is putting the finishing touches on the proceedings of the international symposium on psychiatric research in Asia, held on May 6, 1989, in San Francisco and cosponsored by the Pacific Rim College of Psychiatrists. The committee, through Dr. Sata, will request that APA publish these proceedings.

The committee and the Pacific Rim College of Psychiatrists will propose a joint international symposium on psychiatric research in Asia for the 1991 Hospital & Community Psychiatry Institute. The two groups hope to attract many local and international participants because the Institute will be in Los Angeles.

In response to concerns about refugees, committee member Dr. Paul Leung was asked to write a brief report on the mental health care of Indochinese Americans, particularly concerning service, research, and education. The committee appended his report to the council's May 1990 report to the Joint Reference Committee.

The *Committee of Black Psychiatrists,* Claire M. Cohen, M.D., chairperson, revised its entire charge to clarify the goals and work of the committee.

The committee supported the Committee on Women's proposed position statement on the care of female addicts who are pregnant or have just given birth, especially since many of these women are minorities.

The committee plans to 1) study harassment and violence sparked by the victim's race or ethnicity, 2) recruit black medical students for psychiatry and black psychiatrists for APA, and 3) get information on the effects of toxic waste disposal sites on predominantly minority neighborhoods. The committee will work with the Committees of American Indian/Alaskan Native Psychiatrists, Asian-American Psychiatrists, and Hispanic Psychiatrists on all three tasks and with the Committee on Gay, Lesbian, and Bisexual Issues on the second.

The committee nominated Dr. Evelyn K. Moore for the 1991 Solomon Carter Fuller Award. She is the executive director of the National Black Child Development Institute.

Dr. Diane Felder finished revising the committee's curriculum on black culture and issues.

The *Committee on Foreign Medical Graduates,* Richard Balon, M.D., chairperson, discussed the General Accounting Office's report "Medical Licensing by Endorsement—Requirements Differ for Graduates of Foreign and U.S. Medical Schools." The report pointed out that "regardless of whether documentation requirements are the same for both foreign and U.S. medical school graduates, they pose more difficulty for foreign school graduates." Participants in the round-table discussion held by the American Medical Association (AMA) and the Federation of State Medical Boards agreed that a central clearinghouse to keep and verify information on licensure applicants' educational backgrounds and credentials is desirable. The AMA has established the National Credentials Verification Service to "collect, verify, and maintain documents and credentialing information for physician subscribers preparing to apply for medical licensure and hospital privileges." The committee asked APA to support the establishment of a similar national clearinghouse for *all* graduates of foreign medical schools, whether or not these graduates are AMA or APA members.

Many organizations, including the AMA, now refer to foreign medical graduates as "international medical graduates" (IMGs). The committee feels it is time to change its name because of the prejudicial connotations of "foreign medical graduate." The committee proposed and the council approved changing the committee's name to Committee on International Medical Graduates.

The American Board of Psychiatry and Neurology (ABPN) publishes the pass/fail Board examination results of American medical graduates and foreign medical graduates (FMGs). This information has been used to discriminate against FMGs, and the committee urged APA to ask the ABPN to stop publishing these scores.

Dr. John Kasper, director of the AMA's Department of International Medical Graduates Office of Special Studies, attended the committee's September meeting. He reviewed the work done by his office and the services it offers—"consultative services to members to expand the infrastructure for IMGs, communication with individual IMGs (e.g., about labor relations), close liaison ties with national IMG organizations, and communication of AMA programs and policies to IMGs."

The *Committee on Gay, Lesbian and Bisexual Issues,* Robert Cabaj, M.D., chairperson, reviewed *Report of the Secretary's Task Force on Youth Suicide* (3), Congressman William Dannemeyer's letter to Dr. James Mason of the U.S. Department of Health and Human Services, and Secretary Louis Sullivan's reply. At the committee's request, Dr. Melvin Sabshin wrote to Secretary Sullivan, reiterating APA's 1973 position on homosexuality and human rights.

The committee discussed the problem posed by the position of the U.S. armed services on homosexuality. Since it would take an act of Congress to change the ruling that excludes openly gay men and lesbians from the military and gives the military grounds to discharge them, the committee drafted a position statement that says, "The American Psychiatric Association deplores the exclusion and dismissal from the Armed Services on the basis of sexual orientation." The statement goes on to say that "no burden of proof of judgment, capacity or reliability shall be placed upon homosexuals greater than that imposed on any other persons within the Armed Services."

Another disquieting practice is discrimination against homosexuals by the Immigration and Naturalization Service. It continues to list homosexuality as a mental disorder and can stop an openly gay person from entering the country. APA has tried to have this policy reversed, starting with a letter from Dr. John Spiegel, APA President in 1974, and one from Dr. Melvin Sabshin in 1987. The committee feels that a position statement from APA might help federal legislators who are trying to overturn this policy. It drafted a statement which says that "the American Psychiatric Association deplores the continued inclusion of homosexuality as a mental illness by the Immigration and Naturalization Service; and further deplores the use of this ruling by the Immigration and Naturalization Service for the discriminatory exclusion of homosexual visitors and immigrants to the United States based solely on sexual orientation."

The *Committee of Hispanic Psychiatrists,* Eduardo R. Val, M.D., chairperson, feels strongly that APA, starting with the Council on National Affairs and its components, should take steps to reduce hostility among minorities. Such hostility is evident in academia, in politics, in business, and even in APA. As a start, the committee proposed a meeting of the chairpersons of the minority committees. This would enable them to discuss common problems, goals, and tasks and to consolidate support of position statements, recommendations, etc. It would also foster better understanding of one another's culture and race. In response, the council decided to organize a meeting of all its component chairpersons on Wednesday evening of the fall component meetings.

The committee plans to compile a data base on Hispanic mental health services, which would include psychiatrists, special psychiatric societies, and national organizations that provide such services. Using this data base, the committee plans to write a book. To finance the compilation of this data base, the committee asked permission to seek funds from the National Institute of Mental Health.

The committee nominated Dr. Pedro Ruiz for the 1991 Simon Bolivar Award.

The *Committee on Psychological Aspects of Nuclear Issues,* Stephen Shanfield, M.D., chairperson, asked committee member Dr. David London to update a bibliography on nuclear issues, copies of which are available from the Office of Minority/National Affairs.

At the 1990 annual meeting, the committee presented the symposium "The Psychology of Big Defense Spending." Dr. Perrin French will submit to the council a manuscript based on the papers presented at this symposium with a request that the manuscript be recommended for publication.

The committee is planning "an educational module on nuclear psychiatry for residents." Dr. Jerome Frank suggested that the committee look at the curricula prepared by Psychologists for Social Responsibility and by Educators for Social Responsibility.

The committee had three guests at the September meetings: Samuel W. Lewis, former U.S. ambassador to Israel and current president of the U.S. Institute on Peace, talked about the institute and the Persian Gulf crisis; Michael Mariott, executive director of the Nuclear Resource Information Center, spoke on low- and high-level nuclear waste; and Roger Barnett, Ph.D., vice-president of National Security Research, discussed nuclear deterrents.

The *Committee on Religion and Psychiatry,* Richard Thurrell, M.D., chairperson, discussed the objections to certain passages in "Cults and New Religious Movements," which was a report of this committee. Some Indian psychiatrists took issue with what they saw as "misconceptions about the philosophies, traditions, and religious beliefs of various sects and denominations of Hinduism and Buddhism." They felt that the book "failed to recognize the distinctive cultural patterns and the valid spiritual practices of various Hindu and Buddhist sects and denominations, broadly labeling them all as cults." They cited the labeling of the Hare Krishna religion as a "new religious movement," when in fact it is a denomination (Vaishnavism—"devotees of Vishnu") of Hinduism and goes back thousands of years. The group asked that APA rectify this error and add a section by an expert with Hindu or Buddhist background or by a member from a department of religious study of any American university that teaches Hinduism or Buddhism.

The committee invited Dr. Diana Eck, professor of comparative religion and Sanskrit at Harvard University, who talked about Hinduism and Hare Krishna. The committee benefited from Dr. Eck's visit and plans to study non-Judeo/Christian religions further and perhaps produce a brief but informative handbook on the topic. The committee feels that such a book would be useful to many psychiatrists. The committee will also apologize to the American Association of Psychiatrists from India for the committee's insensitivity.

People have complained to the committee about Christian Psychiatry and satanic cults. Many of the questions and complaints about the latter involve legal and criminal issues. In addition to dealing with these questions and complaints, the committee will ask the district branches to encourage their members to work with local clergy on matters of religion and psychiatry.

The committee nominated Robert Coles, M.D., for the 1991 Oskar Pfister Award.

The *Committee on Women,* Nada L. Stotland, M.D., chairperson, drafted a position statement on the care of female addicts who are pregnant or have recently given birth. The epidemic of substance abuse, especially use of crack cocaine, has resulted in tragic damage to and neglect of users and their children. There has been a recent trend toward prosecution, on the grounds of child abuse, of pregnant and/or postpartum women who use illegal substances, and some penalties involve incarceration, either in prison or in locked psychiatric units. The statement proclaims APA's opposition to the involuntary medical treatment (e.g., Caesarian section) of women on the grounds of fetal welfare and the criminal prosecution and incarceration of pregnant or postpartum women on child abuse charges based solely on substance abuse. It also urges the development of necessary inpatient, outpatient, and residential programs services, including psychiatric care, for these women and their children.

The council approved the position statement in principle, pending review by legal counsel and the Council on Psychiatry and Law, with possible referral to the Council on Addiction Psychiatry and the Council on Children.

The committee hopes to host a women's activity center at the annual meeting in New Orleans, as it did in New York. The center provides a place for female psychiatrists to exchange information and hold special meetings. To finance this activity center, the committee is seeking permission to raise funds outside APA.

Dr. Susan Fiester and Dr. Harold Pincus, Director of the APA Office of Research, briefed the committee on the *DSM-IV* task force's work on late luteal phase dysphoric disorder and self-defeating personality disorder. The Office of Research will send the committee copies of the literature review on the latter and on sadistic disorder.

Dr. Patricia Isbell spoke to the committee about the work of the Council on Addiction Psychiatry and noted the special needs of women with addictions—child care, services for pregnant addicts, and guidance for parents.

The *Task Force on Psychiatric Dimensions of Disasters,* Robert S. Pynoos, M.D., chairperson, met for 4 hours at the New Orleans airport on Oct. 28, 1990. Members Drs. James Black and Raquel Cohen recently organized local and state psychiatric disaster committees. At the meeting of the International Society for Traumatic Stress Studies, Dr. Pynoos collected pertinent information about current national disaster relief organizations and plans, and he has compiled a list of possible national and international consultants to the task force. The task force suggested that, for APA to exert leadership in the formation and implementation of policy on the mental health aspects of planning for and responding to disasters, APA establish liaison with four organizations. 1) The National Disaster Medical System is trying to improve and coordinate medical and surgical response to disasters. 2) The Office of Science and Technology has a National Committee on Disaster Reduction, which is preparing a report for 1991. APA should offer its services to this committee to ensure that mental health aspects are included in the committee's deliberations. 3) The American Red Cross now has a mental health task force, which is studying the psychiatric dimension of disaster recovery. 4) The Federal Emergency Management Agency (FEMA) is involved in the review and reorganization of disaster response plans. The task force also suggested that the district branches form committees on psychiatric dimensions of disasters and work closely with state and local disaster relief groups.

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The Council on Psychiatric Services

J. Frank James, M.D., Chairperson

The Council on Psychiatric Services embodies a strong commitment to the needs of patient populations and the interests of psychiatrist constituencies. In service of that commitment, the council attempts to strengthen and update modalities of care and treatment. These efforts are reflected in the reports of the council and its components.

A number of issues affecting patients with inadequate financial resources took priority in the past year. In September 1990 the Public Citizen Health Research Group and the National Alliance for the Mentally Ill released a report that rated state mental health programs and included a number of assertions and recommendations for public sector psychiatry. The report contained much information that could help those concerned with improving delivery of care and treatment through public systems and facilities. However, two points were particularly troublesome to the council and the Committee on State and Community Psychiatry Systems: first, the assertion that psychiatrists have abandoned the public system and, second, the suggestion that, because of the shortage of psychiatrists in the public system, other nonmedical professionals should be trained to prescribe neuropsychopharmacologic medications. The council believed communication and education are required, particularly for the citizen advocates for the mentally ill. The council emphasized the efforts and role of the Committee on State and Community Psychiatry Systems, APA's project funded by the Pew Memorial Trust to establish collaboration between state systems and universities, the efforts to strengthen the role of medical directors in state mental health agencies and facilities, and the efforts to maintain application of a strong medical standard to state facilities and programs. Near the close of the year, the council was gratified to learn that meetings were planned for discussion of these matters among leaders of APA and the National Alliance for the Mentally Ill.

Access to treatment with clozapine with appropriate monitoring mechanisms was a major concern of the council, which continuously and in concert with other components urged the APA leadership to take action through all possible channels to ensure that patients who may benefit from this medication will have access to it. In May 1990 the Committee on the Chronically Mentally Ill called for rapid attention to the issue by the APA Board of Trustees, and the council again raised the matter in October with the Joint Reference Committee, when concern was expressed by many councils. APA has sponsored forums for communication between psychiatrists and representatives of Sandoz Pharmaceuticals, the U.S. manufacturer of clozapine; it has generated activity and testimony on Capitol Hill; and it has met with representatives of the Food and Drug Administration and representatives of Sandoz. Additional options for action will be explored.

The council supports the principle that psychiatrists have a special responsibility to the mentally ill who cannot pay for services. For several years the council has struggled with how to encourage psychiatrists to provide services for reduced or no fees to poor or underserved groups, a task that is difficult during a time of economic change and uncertainty in the health care field. Nevertheless, the council suggested several mechanisms to encourage and recognize psychiatrists who do provide such services: 1) the district branches could facilitate participation of their members in services for the poor and underserved, 2) APA could recognize district branches whose members make significant contributions, 3) APA could solicit information about exemplary or innovative contributions and give special recognition to the members who make them, 4) APA components could suggest ways in which contributions might be made, and 5) in its communications and negotiations with external groups, APA could promote the development and analysis of data concerning the numbers of indigent or other persons in need of psychiatric care but without the necessary financial resources, the cost-benefits of care, the kinds of care needed, and other information that will allow psychiatry to respond to the needs of those who cannot pay for care. The council's suggestions have not yet been adopted by the Board or Assembly, and the council would welcome ideas from interested members.

In May 1990 the Assembly endorsed an action paper calling for APA attention to the use, adaptation, and development of optimal systems of mental health care delivery. This is a vast topic subject to local laws, conditions, and resources across the country. To get a grasp of the subject, the council agreed to establish a consortium of chairpersons of APA's public psychiatry components. The consortium is charged to identify deficiencies in care delivered to groups with special needs, to present existing or hypothetical models that address such deficiencies in a cost-effective and clinically sound manner, and to prepare information for the APA leadership that could be used for advocacy and other purposes to benefit mental health care delivery systems. The consortium will receive its ongoing direction from the Council on Psychiatric Services. The author of the action paper, Dr. Eric Vance, a psychiatry resident, has been asked to assist the consortium in exploring the possibilities presented by the action paper.

As APA began its efforts to develop practice guidelines, the council recommended that active practicing clinicians be involved from the beginning of the process and have a significant role. Similarly, as APA's Ad Hoc Committee on Managed Care Issues took shape in the past year, the council urged a balance of representation of the different segments of psychiatry, and, at the urging of the Committee on Private Practice, the council emphasized appropriate input from private practitioners.

The *Committee on Private Practice*, Boris Rifkin, M.D., chairperson, continued its efforts to generate information and to examine viewpoints for private practitioners through its column in *Psychiat-*

ric News and through a forum during the 1990 annual meeting that convened private practitioners and several leaders of APA. In conjunction with the Committee on Special Benefit Programs, the committee also sponsored a day of workshops on private practice issues: setting up a private practice, professional liability, legal issues, coping with isolation in private practice, and managed care. The committee expects to sponsor another forum and series of workshops during the 1991 annual meeting. In the past year committee members have arranged liaison with APA components concerning coding and managed care issues to ensure private practitioner input. Because of the committee's full agenda, attempts are under way to add a second Assembly liaison and an additional consultant to the committee.

With support from the Assembly, the *Committee on the Practice of Psychotherapy,* Marcia Goin, M.D., chairperson, worked with the Office of Research to complete a feasibility study regarding the cost-effectiveness of psychotherapy. In this instance, cost-effectiveness is interpreted as dollars saved in the workplace—increased productivity, etc. The result of the study is a report on findings in the literature, problems involved in conducting studies of the issue, and recommendations for next steps. Leaders at the National Institute of Mental Health (NIMH) have expressed interest in the project and are prepared to convene additional meetings with experts in research design, project development, and psychotherapy. Once this is accomplished, it is possible that NIMH will issue requests for proposals for research studies. The committee also continued its work on a brief document for primary care physicians that advocates psychotherapy. The document is now under consideration by the council.

The *Committee on Rehabilitation,* Arthur Meyerson, M.D., chairperson, concerned itself with reports that Medicare intermediaries in some northeastern states began systematic cuts in Medicare funding for rehabilitation/day hospital services. Through *Psychiatric News* the committee solicited information from psychiatrists and other providers who know of instances where Medicare funding was denied on the grounds of lack of active treatment in day care programs. The committee also has worked with representatives of the Task Force on DSM-IV. Particularly, the committee wants users of *DSM-IV* to be aware of the need for specialized disability assessments in diagnostic evaluations for entitlement programs. The committee continues to be APA's liaison to the Rehabilitation Services Administration and the President's Committee on Employment of the Handicapped. Dr. Meyerson represents APA on advisory committees to both of these agencies.

The *Committee on the Chronically Mentally Ill,* Stephen Goldfinger, M.D., chairperson, has expressed strong concern about access to clozapine for appropriate patients and urged the council to raise the issue early in 1990. The committee continues to work with the APA Survey Design and Analysis Department to analyze data obtained in the recent biographical survey concerning chronically ill populations treated by psychiatrists. Working with the Commission on AIDS, the committee is developing a white paper on HIV infection in the chronically mentally ill. The committee expects to discuss issues relating to evaluation of systems of care in the coming year.

The *Committee on State and Community Psychiatry Systems,* Steven Katz, M.D., chairperson, was renamed and reorganized in the past year to increase attention to community psychiatry issues. With the council's full support and through clarification of its charge, the committee renewed its commitment to improve the quality of care for individuals served by public psychiatry, to enhance the effectiveness and image of public sector psychiatrists, and to increase psychiatry's leadership role in public and nonprofit state and community psychiatric facilities and programs. The committee encouraged the district branches to become or continue to be involved in development of their states' comprehensive plans for mental health services, which are updated annually. To add strength to voices calling for improvement in public psychiatry systems and programs, the committee is exploring the development of collaborative relationships with the National Association of State Mental Health Program Directors and the National Council of Community Mental Health Centers.

The *Committee on Liaison With the American Hospital Association,* Stuart Keill, M.D., chairperson, continues to meet with its counterpart from the American Hospital Association. The joint committee of the two associations reviews recent and anticipated legislation and regulations to alert the parent organizations of shared interests and concerns. This year, the joint committee studied the impact of various managed care programs on the delivery of psychiatric care by hospitals. The committee also urged APA to expeditiously develop psychiatric clinical indicators for hospital quality assurance programs that would reflect current psychiatric treatment practices, be easily adapted by hospital-based psychiatrists, and be easily comprehended by the staff of accrediting bodies. The committee noted that the Health Care Financing Administration and the Joint Commission on Accreditation of Healthcare Organizations are creating their own such indicators.

The *Institute on Hospital & Community Psychiatry Program Committee,* James T. Barter, M.D., chairperson, developed an exciting and rich program for the Institute in Denver on Oct. 7–11, 1990. The Institute's theme was "Emerging Issues in Clinical Psychiatry," and it included full-day sessions on AIDS, managed care, dual diagnosis, and women's treatment. Fourteen allied mental health groups held meetings, and APA sponsored a forum on clozapine titled "Clozapine: Indications, Access, Availability, and Research," which elicited considerable input and discussion. Harold Eist, M.D., is chairperson of the program committee for the 1991 Institute, and the committee has begun planning for that meeting, which will be in Los Angeles on Oct. 20–24.

The *Committee to Coordinate the Functions of the H&CP Service, Journal, and Institute,* Gail Barton, M.D., chairperson, asked for and was granted a shorter name. Although its charge has not been changed, it will now be known as the Committee on the H&CP Service. This committee reported that the Service has transferred substantial funds to the *H&CP* journal to support Service members' subscriptions. The Psychiatric Placement Service, a component of the H&CP Service, was organized to help hospitals and systems find qualified psychiatrists for vacant positions. Although this service is available to all facilities, Service members are charged a lower fee. The *Video and Film Library Catalog,* listing videos available for rent from the H&CP Service, was published in October; 22 new videos have been added to the library. The Service also added two new publications: *Collected Reprints From an H&CP Special Issue on Clozapine* (1) and *Video and Film Reviews* (2), edited by Ian Alger.

The *Committee on Veterans' Affairs,* Frederick Guggenheim, M.D., chairperson, obtained endorsement by the APA Board of Trustees of several statements that can be used to support advocacy for psychiatric patients cared for by the U.S. Department of Veterans Affairs (VA). These statements call for the availability in VA programs of a full range of services, from long-term outpatient care to short-term inpatient intensive care. To address the psychiatric staff shortage, APA supported new affiliations between VA psychiatry services and academic departments of psychiatry and cooperative cost-sharing agreements that involve scarce personnel and high-technology devices. APA also emphasized the importance of research to the recruitment and retention of physicians in the VA and in the maintenance of quality services to VA patients. The committee appreciated the excellent support of the APA Division of Government Relations, which prepared testimony for hearings throughout the year.

The *Committee on Psychiatric Services in the Military,* Harry Holloway, Jr., M.D., chairperson, expressed its concern about the proposal by the Department of Defense to allow nonphysician mental health professionals to prescribe neuropsychopharmacologic agents after a brief training period. APA believes that such privileges, without proper medical training, would lead to at least inadequate patient care, if not harm. APA has energetically and repeatedly tried to influence the Department of Defense and Congressional committees and to inform them about the effects of these medications and the education and complex training needed to prescribe them. With regard to Operation Desert Shield, the committee urged psychiatrists to volunteer services for those directly involved in the activity in the Persian Gulf and for members of their families, and the APA Board of Trustees joined in this encouragement. In another area, the committee noted that APA had enacted a policy to ban recruiters from its meeting exhibits if the sponsor discriminated in its employment practices on the basis of several factors, including sexual orientation. The committee pointed out that while this policy ultimately affects the psychiatric staff in the military, it has little effect on the overall policies of the Department of Defense, which are determined by Congress. The committee suggested that more definitive progress might result from political efforts to change public laws and regulations.

The *Task Force on the Homeless Mentally Ill,* Frederic Kass, M.D., chairperson, developed an interim report titled "General Directions for Public Policy in Behalf of the Mentally Ill Among the Homeless Population," and the Board approved its publication. The report emphasizes the range of services, including comprehensive psychiatric services, needed to help homeless mentally ill individuals. The report can be obtained from the Office of Psychiatric Services. The task force continues to work on reports on homeless children and families, women, and other at-risk populations. The task force is also gathering information about district branch involvement in local projects in behalf of the homeless mentally ill.

The *Task Force on Psychiatric Services for Mentally Retarded/Developmentally Disabled Adults,* Ludwik Szymanski, M.D., chairperson, completed its report and recommended increased attention by psychiatrists to this special population. Mental retardation is not limited to children, and the overwhelming majority of retarded adults living in the community use generic community facilities. Many have jobs, ranging from sheltered workshops to competitive employment. While living in the community upholds the rights and dignity of retarded persons, it exposes them to the stresses of modern life and others' expectations of certain behaviors. The task force stressed that retarded persons have the same mental disorders as nonretarded people, and these can be diagnosed with the standard diagnostic criteria and techniques modified to fit the patient's communication level. The report can be obtained from the Office of Psychiatric Services. The task force has also proposed establishment of a committee on psychiatric services for the mentally retarded to develop liaisons and projects for ensuring greater psychiatric input and involvement in services to the mentally retarded.

The *Task Force on Clinician Safety,* William Dubin, M.D., chairperson, reported that interest and concern about clinicians' safety is high, as documented by the number of inquiries from the press, media, residents, other psychiatrists, professionals from other disciplines, district branches, and state officials. The task force has been as responsive as possible to these inquiries. It sponsored several programs during the APA annual meetings, gathering information and following up by interviewing psychiatrists who identified themselves as having been assaulted or threatened. The task force anticipates completion of its report in the near future.

Two components began work during the year. The *Committee on Psychiatric Services in Jails and Prisons,* Henry Weinstein, M.D., chairperson, is charged to develop curricula for education, to enhance practitioners' opportunities for professional development in this area, and to advise APA components, national organizations, and others on matters relating to mental health issues involving jails and prisons. The *Task Force on Family/Systems Therapy,* Frederick Gottlieb, M.D., chairperson, is charged to identify specific family/system issues appropriate for APA concern and action and to develop a succinct working document for APA components that can be used to frame liaison activities within and beyond APA.

In June 1990 the council formally recommended, and the Board of Trustees approved, the disbandment of two long-standing components, the *Committee on Drug Abuse,* Edward Kaufman, M.D., chairperson, and the *Committee on Alcoholism,* Richard Frances, M.D., chairperson. Both committees were commended for their excellent work, development of positions and reports, and support for establishment of the APA Council on Addiction Psychiatry, which will have an opportunity to expand APA's work in this field.

It has been a busy and rewarding year. The council anticipates several challenges in the coming year relating to access to services, quality of care, and the strength of psychiatry's contribution in the many arenas touching on treatment and services.

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The Council on Psychiatry and Law

Paul Appelbaum, M.D., Chairperson

In December 1989 the APA Board of Trustees approved a resource document concerning patients' right to refuse medication. This document was approved with the proviso that the council would review the experiences in the states that had mandated judicial review for refusals of medication in order to understand the problems and any possible benefits. At its fall 1990 meeting the council reviewed an informal survey of the 13 states that maintain a judicial review mechanism. The survey was based on the experiences of a hospital administrator and a clinician from each of the 13 states. The council has appointed a subcommittee that will draft a short paper to supplement the right to refuse medication document. The proposed paper will focus on the disadvantages and advantages of judicial review systems and will suggest ways to maximize the benefits of those systems. The paper will not contain a proposal for model regulations for organizing state judicial review systems. It is expected that a draft of the paper will be available to the Council for review at its May 1991 meeting.

During its May 1990 meeting the council heard from APA staff about recent investigations and prosecutions involving Medicaid fraud. The investigations have focused on three major issues: 1) the tendency among enforcement units to resort to prosecution before pursuing available civil remedies, 2) the intrusive investigatory techniques that are widely used by these enforcement units, and 3) the ambiguity within the regulations themselves concerning proper coding and billing practices for psychiatrists. As a follow-up to this briefing, Dr. Appelbaum, along with the chairpersons of the Joint Commission on Government Relations and the Commission on Judicial Action, drafted a letter to the district branches. This communication outlined the problem and asked the district branches to attempt to clarify at the state level the regulations and the enforcers' interpretations of them.

The council has been examining the reporting of mentally ill persons to departments of motor vehicles. In the meantime, Jeffrey Metzner, M.D., a council member, was asked by the Federal Highway Administration to chair a task force to determine standards governing the issuance of drivers' permits to mentally ill persons.

The federal task force is expected to complete its final report by October 1990. Once the work of the Federal Highway Administration is completed, Dr. Metzner will formulate a proposal on APA's role in this area. This proposal will be considered by the council at the May 1991 meeting. At that time the council will discuss whether to propose an APA task force to study this issue.

In an effort to determine a mechanism for peer review of forensic testimony, the council met with the Commission on Judicial Action during the fall components meetings. The groups reviewed deposition and trial testimony submitted by two members of the council. The goal of the project was to determine whether groups of psychiatrists could meaningfully evaluate colleagues' testimony. The council members agreed this particular experiment proved that educational peer review is clearly possible when transcripts are not problematic, as was the case here. The next step is to determine whether peer review is possible when testimony raises issues of ethics or competence and, if so, what contribution such a review can make. The council will meet with the Commission on Judicial Action at the May 1991 meeting to pursue this issue.

The desirability of legislation criminalizing psychotherapist-patient sex was the subject of a preliminary discussion at the council's fall meeting. The council decided to invite representatives from other appropriate components for further discussion of this issue.

The *Committee on Confidentiality,* Renee Binder, M.D., chairperson, has continued to address confidentiality concerns brought to its attention by APA components and members. At the instruction of the Joint Reference Committee, the committee coordinated responses by various APA components to an Area III Assembly action paper, "The Role of the Psychiatrist When Requested to Provide Information About Patients for Security Clearances." After reviewing the components' responses, the committee drafted (and the council approved) a set of guidelines, which read,

> 1) A current authorization to release information should be included with any such request for information.
>
> 2) In addition, to be certain that the authorization represents an informed consent, the psychiatrist should make reasonable efforts to contact the patient directly and discuss the information to be released and the possible consequences of its disclosure.
>
> 3) As with other requests for release of information, care should be taken to limit the information released to that which is relevant to the request.

These guidelines were approved by the Joint Reference Committee at its October meeting and will be forwarded to the Assembly and Board for their approval.

The committee met with staff from *Psychiatric News* to discuss the possibility of a column every 2 months. The column would have a question-and-answer format and would initially focus on third-party evaluations and confidentiality.

Other topics the committee is currently discussing include confidentiality in residency training programs and the confidentiality of computerized records.

The *Task Force on Disclosure of Psychiatric Treatment Records in Child Custody Disputes,* Carl Malmquist, M.D., chairperson, continues to develop a report on issues involving access to a parent's psychiatric records in child custody disputes.

The *Task Force on Use and Misuse of Psychiatric Diagnoses in the Courts,* Seymour Halleck, M.D., chairperson, hopes to have a final draft of its report by May 1991. The document covers the appropriate use of psychiatric diagnoses and is intended to assist the courts in avoiding over- or understatement of the importance of diagnosis in reaching a judgment about a person's mental state. The report also is an attempt to deal with the difficult issues of the concept of disease and its implications for responsibility for behavior.

The *Task Force on Consent to Voluntary Hospitalization,* Francine Cournos, M.D., chairperson, is a new task force formed as a result of the Supreme Court decision in *Zinermon v. Burch.* This decision raised questions about the legitimacy of consent given by patients who may be incompetent at the time of hospitalization and suggested that such patients should be dealt with by means of involuntary commitment. This task force will 1) review the *Zinermon* decision and other applicable law, 2) assess the impact *Zinermon* has already had on state mental health systems, 3) recommend options for APA and its district branches to pursue, through regulatory and legislative channels, to maintain a viable system for voluntary hospitalization, and 4) embody those options in a report that can be used as background material for policy makers considering changes in procedures for voluntary hospitalization.

The Council on Research

Herbert Pardes, M.D., Chairperson

The Council on Research, in conjunction with its components, is the body within the Association that ensures the vigor of the psychiatric research enterprise by focusing on science policy and scientific assessment, research studies, and, especially important, research training. The council has been carefully monitoring science policy issues, particularly animal rights, research appropriations, conflict of interest, training and infrastructure needs, and funding of research on child psychiatry. Many of these issues and those of the research components are addressed in the column "News From the Council on Research" in *Psychiatric Research Report* (*PRR*), the Office of Research quarterly newsletter. Individuals who would like to receive *PRR* should contact the APA Office of Research.

The council was delighted to meet and continue its annual discussions with key leaders of the federal research agencies, including the Alcohol, Drug Abuse, and Mental Health Administration, the National Institute of Mental Health (NIMH), the National Institute on Alcohol Abuse and Alcoholism, and the National Institute on Drug Abuse. Over the years these meetings have identified issues of mutual concern and provided an opportunity for informal collaboration. Areas that were highlighted this year include Decade of the Brain activities, the implementation of the child mental disorders research plan, the reorganization of NIMH, 1991 research appropriations, drug abuse clinical research guidelines, and animal research, among others.

Animal research remains high on the council's agenda, and the council continues to stress the need to educate the public about the essential role of animal research in the clinicial neurosciences. In addition to monitoring federal regulations concerned with this issue, this year the council recommended to the Board of Trustees that contributions be made to two important organizations—the Coalition for Brain Research and the Medical Society Legal Defense Fund. The coalition is composed of representatives from the major clinical societies involved in brain and behavioral research, and it produces and develops patient and other needed educational materials. The Medical Society Legal Defense Fund assists scientists who have legal difficulties resulting from actions by animal rights activists. In addition to pledging a portion of its own budget and requesting matching funds from other APA sources, the council will alert other psychiatric groups (e.g., the American College of Neuropsychopharmacology, the American Association of Chairmen of Departments of Psychiatry, the American Academy of Child and Adolescent Psychiatry, the American Psychosomatic Society, the American Psychopathological Society, the American Psychological Society, and the Biological Psychiatry Association) to the important work of the Coalition for Brain Research and the Medical Society Legal Defense Fund.

The council collaborates regularly with the Scientific Program Committee, and its efforts have helped to increase the size of the New Research Program, which doubled in 1990. The Young Investigator sessions and activities have gone very well since they were initiated in 1989, as have the other research sessions.

The council administers two APA awards—the Lilly Psychiatric Research Fellowship and the Kempf Fund Award for Research Development in Psychobiological Psychiatry. The council reappointed last year's award subcommittee (Ron Rieder, M.D., Robert Cancro, M.D., Robert Hirschfeld, M.D., and Walter Hong, M.D.) to review the 1991 applications and select the winners. The winners of the 1990 Kempf award were John Kane, M.D. (senior awardee) and Gustav Degreef, M.D. (junior awardee), and Christopher McDougle, M.D., received the Lilly Psychiatric Research Fellowship.

The final report of the *Task Force on Prevention Research,* Robert Rose, M.D., chairperson, was approved and published in the *American Journal of Psychiatry* (1). The task force was discharged and thanked by the Board of Trustees when the report was approved in June 1990.

The *Committee on Research on Psychiatric Treatments,* John Kane, M.D., chairperson, spent considerable time discussing the development of practice guidelines and convened a meeting early in 1990 primarily to assist APA in framing the overall plan for addressing this issue. The committee considered and suggested options with regard to several practice guideline areas, including the nature of the guidelines, the process of development, and policy considerations. The committee stressed that any practice guidelines developed must be based on evidence and well documented, that they must involve clinician input, and that the APA efforts should not encourage pseudospecificity in the absence of meaningful data. The minutes of this early meeting were subsequently used as a starting point for the joint Board and Assembly Work Group on Practice Guidelines that was later appointed by the Board of Trustees. The committee and the council agreed that development of practice guidelines is a complex task and that the guidelines will have a major impact on the practice of psychiatry, and they strongly urged that, to assure credibility of the final product, the project be placed under the aegis of the Council on Research.

Additional activities of the committee include revising the psychopharmacology screening criteria that were published in the last edition of the peer review manual; the revised criteria will be published in the next edition. The committee actively discussed many of the controversial issues involving clozapine and agreed in October to set up a small subcomponent to develop criteria for alternative monitoring systems. Other issues considered by the committee were anticonvulsants in psychiatry, treatment of nicotine dependence, and the nursing home guidelines for use of psychiatric drugs developed by the Health Care Financing Administration.

Further, the Committee on Research on Psychiatric Treatments oversees a variety of treatment-related task forces, including the Task Force on Electroconvulsive Therapy, the Task Force on Benzodiazepine Dependency, the Task Force on Psychosocial Treatment Research, and the Task Force to Study the Long-Term Effects of Lithium on the Kidney. Summaries of their activities are included in the component reports that follow.

The *Task Force on Tardive Dyskinesia,* John Kane, M.D., chairperson, submitted its final report to the Committee on Research on Psychiatric Treatments, the Council on Research, and the Joint Reference Committee in the fall of 1990. The report was approved by each of these groups pending a few nonsubstantive changes. If approved by the Board in December 1990 the report will be published as an APA task force report. The Council on Research agreed that the report was comprehensive and generally an excellent educational document and will likely be widely quoted.

The council was pleased that the report of the *Task Force on Electroconvulsive Therapy,* Richard Weiner, M.D., chairperson, titled *The Practice of Electroconvulsive Therapy: Recommendations for Treatment, Training, and Privileging* (2), was well received in the psychiatric community and continues to sell well for APA. The task force responded vigorously to proposed regulations published by the Food and Drug Administration (FDA) to reclassify ECT devices from class III (requiring premarket approval) to class II (requiring a performance standard) for use in treating severe depression. The task force, working in conjunction with the Division of Government Relations and through coordinated activities with other groups and individual psychiatrists, hopes to persuade the FDA to modify the regulations to include mania and schizophrenia in this reclassification and to clarify the meaning of "severe depression."

The *Task Force on Psychosocial Treatment Research,* John Docherty, M.D., chairperson, submitted a draft of its final report to the Committee on Research on Psychiatric Treatments. The committee reviewed the document and requested that a number of changes be incorporated before the report is forwarded to the council. The council anticipates that the document will be approved for publication sometime in 1991.

The council recommended that the *Task Force to Study the Long-Term Effects of Lithium on the Kidney,* George Heninger, M.D., chairperson, be dismissed. While the task force report itself was never completed, because of a variety of difficulties, the current evidence indicates that lithium has no clinically significant long-term effects on the kidney.

The report of the *Task Force on Benzodiazepine Dependency,* Carl Salzman, M.D., chairperson, was published early in 1990 and is available from the American Psychiatric Press, Inc. The council was very pleased with the document, *Benzodiazepine Dependence, Toxicity, and Abuse* (3), but, as the task force had completed its work, the council recommended that it be disbanded with thanks and acknowledged for its excellent contribution to the literature.

The *Committee on Research Training,* Ronald Rieder, M.D., chairperson, is focusing on both long-term and short-term recruitment of researchers. It has developed a clearinghouse to assist medical students, residents, and psychiatrists with finding appropriate training programs and to disseminate information that will support development of psychiatric research careers. The committee currently is working on a proposal for the development of research tracks to be incorporated into psychiatric residency training programs. It hopes to accomplish this by establishing flexible guidelines for research training tracks and suggesting how they can be integrated into the Residency Review Committee requirements, compiling and disseminating detailed information about programs offering such tracks, and using the National Resident Matching Program for delineation of these tracks. Under the National Resident Matching Program, research tracks would be delineated with a specific match number (i.e., a unique suffix would be used to indicate that a specific facility has a psychiatric research training track). This system would identify and promote these tracks to science-minded applicants who might not have otherwise realized such programs are available. The committee hopes to develop such a program by working with the American Association of Chairmen of Departments of Psychiatry, the American Association of Directors of Psychiatric Residency Training, the Committee on Graduate Medical Education, the Residency Review Committee, and other groups. A copy of the committee's proposal is available from the APA Office of Research.

A longer-term proposal being considered by the committee is the initiation of a national conference on recruitment. The plans for this conference, however, have been suspended while the committee concentrates on the research track proposal.

The committee maintains an important liaison with the Advisory Committee for the Program for Minority Research Training in Psychiatry, since the goal of this program is to increase the number of underrepresented minority men and women in psychiatry research. Under this program, funding was granted to six "mini-fellows" for attendance at the annual meeting of the Southern Association for

Research and Psychiatry, which took place in Chapel Hill, N.C., in March 1990. In addition, 20 more "mini-fellows" received funds to attend the 1990 APA annual meeting, and plans are under way to support the attendance of 10 APA "mini-fellows" at the American College of Neuropsychopharmacology meeting in December. Other aspects of this program include recruitment, the establishment of data bases and networks, and the development of systems to fund additional research training experiences for medical students, residents, and postresidency fellows. The advisory committee will be discussing the availability of funding for minority faculty at a future meeting. Additional information on the Program for Minority Research Training in Psychiatry is available from the APA Office of Research.

The *Committee on the Biographical Directory and Research on Psychiatric Professional Activities,* Robert Dorwart, M.D., chairperson, reports that the *1989 Biographical Directory* has sold more than 3,500 copies since it was published in 1989. However, the directory was expensive to produce and consistently loses money, so the committee is exploring a number of options for publication of future directories and will present several to the council for its consideration next fall. Specifically, the committee believes that a smaller, less expensive, more up-to-date directory may be needed. Most research data would then be collected through smaller surveys of specifically targeted samples separate from the directory process. The committee developed and distributed an errata sheet for the 1989 directory.

The committee continues to analyze the data collected from the professional activities survey and has provided data to the Committee on the Chronically Mentally Ill and to the Task Force on Psychiatrist Payment for the study of specific topics. The committee is also writing an article describing basic findings from the professional activities survey, and it is collaborating with researchers at Harvard University and the University of Maryland to rapidly analyze and disseminate professional activities survey findings concerning important policy issues to APA and the field.

The *Work Group on National Data Bases for Psychiatry,* Robert Dorwart, M.D., chairperson, reports directly to the Board of Trustees but maintains an important liaison with the Council on Research. This group is developing a preliminary report that will be shared with the council early in 1991 so the council can use the information in it.

The *Committee on Psychiatric Diagnosis and Assessment,* Layton McCurdy, M.D., chairperson, oversees diagnostic assessment activities, including the work of the Task Force on DSM-IV and the Task Force on Quantitative Electrophysiological Assessment (separate reports follow). In addition to overseeing these important components, the committee examined the effectiveness of diagnostic testing and therapeutic services for sleep disorders, recommended that APA adopt a policy on DSM-related computer software, and has been involved in the American Board of Psychiatry and Neurology's development of a process for granting special qualifications in EEG to psychiatrists.

The final report of the *Task Force on Quantitative Electrophysiological Assessment,* Robert Freedman, M.D., chairperson, was approved by the Committee on Psychiatric Diagnosis and Assessment, the Council on Research, and the Joint Reference Committee and has been forwarded to the Board of Trustees for approval. The council generally agreed that the report was excellent. Basically, it indicates that quantitative EEG has some limited utility clinically as an adjunct in diagnosing certain disorders, such as delirium and dementia, involving significant CNS dysfunction. While it is a valuable research tool for investigating other psychiatric disorders, its clinical utility in this regard has yet to be demonstrated.

The *Task Force on DSM-IV,* Allen Frances, M.D., chairperson, reported that the development of *DSM-IV* is going extremely well. Each work group developed a literature review, and these reviews have been widely distributed. The John D. and Catherine T. McArthur Foundation provided grants for the reanalysis of data and for general field trials. In addition, NIMH has funded focused field trials, which are now under way. *DSM-IV Work in Progress: Options Book* will be available in the spring of 1991. The task force is also developing a primary care *DSM-IV* effort and has contacted primary care specialty groups to have formal liaisons appointed. The Committee on Consultation-Liaison Psychiatry and Primary Care Education has also been actively involved with this effort. Finally, the task force produces *DSM-IV Update,* a semiannual newsletter. Individuals wishing to receive copies should write to the APA Office of Research.

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THE AMERICAN JOURNAL OF PSYCHIATRY

Editorial

Whatever Happened to Insomnia (and Insomnia Research)?

National surveys of the prevalence of insomnia have always reported impressively high numbers of Americans with complaints of insomnia. In a study of the 1-year U.S. prevalence of insomnia reported at the 1983 National Institute of Mental Health (NIMH) Consensus Conference on Drugs and Insomnia (1), 33% of the Americans surveyed complained of insomnia to some degree and 17% of this group reported that their symptoms were serious. Only 15% of the subjects with serious insomnia in this survey used prescribed or over-the-counter hypnotics. Nevertheless, three different hypnotic drugs were listed among the top 200 best-selling drugs of 1989 (2).

Despite the vast number of patients with complaints of insomnia and the fact that symptoms of insomnia are among the most common complaints in the doctor's office, research on the etiology and treatment of insomnia has not reflected its high frequency or substantial impact on the patient. A search of currently funded NIMH grants revealed only four projects dealing primarily with the pathophysiology, diagnosis, or treatment of insomnia. It is even more discouraging that Reynolds and colleagues, reporting in this issue of the *Journal* (3), could find only 27 research studies of primary insomnia published during the last 20 years that met minimal standards of empirical research. Their article is an important step in the path to developing useful, reliable, valid, and specific diagnostic and treatment strategies for insomnia. As extensively described in their article, clinical wisdom and experience have far outstripped the supporting published empirical evidence in insomnia diagnosis and treatment. Therefore, diagnostic and treatment decisions may lack specificity and reliability or may even not have a firm basis in fact.

Their review deals with primary insomnia, a category of insomnia that is not associated with diagnosable mental disorders (or medical disorders). Indeed, in the U.S. survey just described (1), 50% of the group with serious insomnia did not report high levels of emotional distress. This is consistent with the evolving concept of insomnia as a multifactorial disorder that may be caused and maintained by organic, psychological, and/or other factors. The idea that insomnia is not necessarily psychological has been reflected in changes in *DSM-III* and *DSM-III-R* and in the 1979 sleep nosology of the Association of Sleep Disorders Centers (4) (currently the American Sleep Disorders Association) and the newly published *International Classification of Sleep Disorders* (*ICSD*) (5), also published by the American Sleep Disorders Association in collaboration with several international sleep research societies. The first *DSM* editions categorized insomnia in a manner suggesting its etiology is purely psychological. However, by the late 1970s, with the explosive development of sleep disorders medicine as a clinical and research discipline, it was clear that some insomnias were caused, maintained, and/or exacerbated by organic disorders. This was documented in depth by the ground-breaking 1979 sleep nosology. Despite some controversy, it was considered to be sufficiently important to be included in outline form as an appendix in *DSM-III*. *DSM-III-R* included a section on sleep disorders in the main body of the text and is notable because for the first time it acknowledged that insomnia may be related to a known organic disorder.

The fact that insomnia may be associated with mental, organic, or other factors should have a dramatic impact on the differential diagnosis and treatment of insomnia (6). As noted in the NIMH consensus conference, it is incumbent on the practitioner to search for any underlying mental or organic cause of insomnia so that the therapy chosen is appropriate. In addition to sedative/hypnotics, the following types of treatment have been reported to be useful for insomnia: progressive relaxation training; electromyographic (EMG), theta, or sensorimotor rhythm (SMR) biofeedback training; behavioral therapies, including stimulus control and sleep restriction therapy; and therapies for insomnia with clear organic etiologies, such as nasal continuous positive airway pressure (NCPAP). Unfortunately, the treatment literature indicates a heavy emphasis on hypnotic medications for the treatment of insomnia. This emphasis on hypnotic medication research may simply reflect a lack of general information regarding the causes of insomnia and available nonpharmacological treatments. Alternatively, it may result from a lack of research regarding the best treatments for different types of insomnia or a greater availability of research funds in this area from pharmaceutical companies.

Insomnia is typically reported to be unpleasant and frustrating, to provoke anxiety, to induce sleepiness, and even to be disabling, yet it is often seen as an unavoidable and normal part of life. Progress in the diagnosis and treatment of insomnia may be hindered by the general perception by patients and doctors alike that insomnia is common, usually transient, and trivial. Physicians and other mental health professionals have also experienced insomnia themselves and may have preconceived notions about its causes and treatments.

The article by Reynolds and colleagues in this issue of the *Journal* points the way for much needed research in insomnia. The authors have showed courage in rejecting some of the *ICSD* primary insomnia categories for inclusion in *DSM-IV* even though they are currently used by many sleep disorders clinicians. However, by rejecting them because of insufficient empirical evidence, they have set a high standard for inclusion of future new categories in *DSM-IV* and signaled that clinical experience and judgment must be supported by unbiased, well-controlled research. Better diagnoses will allow the clinician to select treatments most appropriate to the symptom picture.

Insomnia has serious effects on many patients' lives. Continued research efforts must complement clinical wisdom if the current knowledge in insomnia diagnosis and treatment is to progress beyond the "take two of these at bedtime" level of practice.

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Origins of *DSM-I:* A Study in Appearance and Reality

Gerald N. Grob, Ph.D.

The author traces the history of psychiatric nosology in the United States from its origins in the early nineteenth century to the introduction of DSM-I *in 1952. Until World War I, psychiatrists were not interested in systematic classification, although they were concerned with diagnosis. The first official nosology, adopted in 1918, reflected the need to collect mental hospital data. The federal Bureau of the Census had a role in the development of this nosology in that it required such data. The publication of* DSM-I *marked an internal transformation that mirrored the growing dominance of psychodynamic and psychoanalytic psychiatry and the relative weakness of the biological tradition. This transformation occurred largely as a result of the lessons learned by psychiatrists during World War II. The author's basic argument is that nosology reflected not only psychiatric ideology but also other, external determinants at any given point in time.*

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In modern medicine, as in modern society, classification systems play a crucial role, for without such systems the collection and analysis of data are all but impossible. Two symbols perhaps best represent the centrality of taxonomy: the census and the computer. In its origins, the census was but a limited undertaking designed for certain specific purposes: to facilitate the collection of taxes, to measure the strength of the nation-state, or to allocate political representation. In the nineteenth century, however, a radically new concept emerged, namely, that the census could define and describe reality in statistical terms. Similarly, the computer was given legitimacy by the appealing claim that it was both possible and desirable to group data of all varieties into logical and self-evident categories. In turn, the analysis of the relationships among different classes of data could lead to greater knowledge and understanding, whether of the social and physical environment or of human behavioral patterns.

Classification systems are neither inherently self-evident nor given. On the contrary, they emerge from the crucible of human experience; change and variability, not immutability, are characteristic. Indeed, the ways in which data are organized at various times reflect specific historical circumstances. Empirical data, after all, can be presented and analyzed in endless varieties of ways.

The development of psychiatric nosology is a case in point. Although nosological debates dealing with mental disorders were (and are) phrased in scientific and medical language, they were shaped by a variety of factors: the social origins and ideological, political, and moral commitments of psychiatrists; their desire for status and legitimacy; the characteristics of their patients; the nature and location of their practices; and the broader social and intellectual currents prevalent at a given time. Nowhere are these generalizations better illustrated than in the developments that culminated in the publication of the first edition of the *Diagnostic and Statistical Manual: Mental Diseases* (*DSM-I*) in 1952.

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NOSOLOGY VERSUS DIAGNOSIS

Psychiatrists in nineteenth-century America were for the most part uninterested in elaborate nosologies that systematized mental illnesses in formal and overly rigid ways. Like other physicians, they conceived of disease in individual rather than general terms. Health was a consequence of a symbiotic relationship or balance among nature, society, and the individual (1, 2). Disease, by way of contrast, represented an imbalance that followed the violation of certain natural laws that governed human behavior. To be sure, mental illnesses were indistinguishable from other physical illnesses and occurred when false impressions were conveyed to the mind because the brain or other sensory organs had been impaired. Nevertheless, psychiatrists also believed that mental illnesses were precipitated by a combination of psychological and environmental etiological factors that were mediated by the constitution or predisposition of the individual. Thus, insanity often followed violation of the natural laws that governed human behavior and was linked as well with immorality, improper living conditions, or other stresses that upset the natural balance.

The holistic concept of insanity for American psychiatrists represented both an act of faith and a starting assumption. Except for a few cases in which autopsies revealed the presence of a brain tumor or other physical abnormality, the link between organ and behavior remained shrouded in mystery. Given their inability to demonstrate a relationship between anatomical changes and behavior, psychiatrists identified mental disorders by observing external signs and symptoms. In this respect they were no different from other physicians. Prior to the conceptual changes that began to transform medical thought in the late nineteenth century (symbolized by the specific germ theory of disease), most practitioners defined pathological states in terms of external and visible signs (such as fever). To infer pathology by focusing on signs admittedly created serious intellectual and scientific problems; the preoccupation with differentiating among various fevers was but one striking example. Although disagreeing on the diagnosis of signs and symptoms, few physicians questioned this approach, if only because other alternatives were largely lacking. Similarly, nineteenth-century psychiatrists accepted disease as a given; the inability of patients to function, combined with severe behavioral symptoms, was sufficient evidence of the presence of pathology.

Classification systems based on symptoms created grave and perhaps insoluble problems, thus reinforcing psychiatrists' lack of interest, if not hostility, toward nosology. What kind of classification system could possibly encompass the innumerable and protean forms of abnormal behavior? No system of classification, conceded Amariah Brigham in 1843 (3), appeared to be of "much practical utility"; all categories based on symptoms "must be defective, and perhaps none can be devised in which all cases are arranged." Nor were Brigham's views unique. Samuel B. Woodward (4), Superintendent of the Worcester State Lunatic Hospital and first President of the Association of Medical Superintendents of American Institutions for the Insane (now APA), had observed earlier that insanity was a "unit, indefinable . . . easily recognized . . . [but] not always easily classified." Indeed, he believed that therapy was independent of any nosological system but, rather, had to reflect the unique circumstances presented by each individual case (4–8).

To suggest that American psychiatrists were not persuaded that a systematic nosology was crucial to their practice is not to imply that they were unconcerned with diagnosis. On the contrary, they recognized the importance of classification and even engaged in fierce debates over the validity of such specific categories as moral insanity (9) (a condition in which there was a morbid perversion of the emotions but little or no impairment of the thought process or the intellect) and the relationship of broad psychiatric categories associated with homicidal insanity (10). However, they also were acutely aware of the formidable barriers that blocked the development of all-encompassing systems. Hence, their nosologies tended to be general and fluid, and judgments about individual patients represented pragmatic choices that had few practical consequences. In 1838, in his classic treatise on the medical jurisprudence of insanity, for example, Isaac Ray (11) followed J.E.D. Esquirol's classifications and divided insanity into two broad groups. The first—idiocy and imbecility—included individuals with congenital defects. The second encompassed those in whom lesions had impaired the functioning of the mind and included mania (either intellectual or affective) and dementia. Ray, as a matter of fact, denied that any classification could be "rigorously correct, for such divisions have not been made by nature and cannot be observed in practice." Diseases, he added, "are naturally associated into some general groups only; but if these be ascertained and brought into view, the great end of classification is accomplished."

If psychiatrists recognized that nosology was not critical to clinical practice, they were cognizant of its role in the collection of statistical data. After 1800, a number of currents had given rise to a type of social inquiry whose methodological distinctiveness was a commitment to quantitative research. Underlying the application of quantification was the assumption that such a methodology could illuminate and explain social phenomena. Nineteenth-century American psychiatrists were deeply committed to the collection and analysis of such data. In their eyes, statistical inquiry could shed light on recovery rates, uncover the laws governing health and disease, serve the ends of policy advocacy, and enhance the legitimacy of both their specialty and their hospitals (12).

The collection of statistical data, of course, required categories. Most of the categories used by nineteenth-century psychiatrists, however, dealt with the demographic characteristics of patients as well as admission and discharge rates; nosology occupied a distinctly subordinate position. At the International Congress of Alienists in 1867 (13), for example, a commission dealing with psychiatric statistics recommended a broad system that involved only seven categories of insanity (simple, epileptic, paralytic, senile dementia, organic dementia, idiocy, and cretinism). The focus of their report, nevertheless, was on demographic rather than nosological variables. When the document was brought before the Association of Medical Superintendents of American Institutions for the Insane in 1869 (14), the focus remained unchanged. Some years later, Clark Bell (President of the New York Medico-Legal Society and a delegate to the International Congress on Psychiatry and Neurology in 1885) asked a group of psychiatrists to prepare an American nosology. In response, a small group (15, pp. 372–377) simply followed their British brethren and identified only eight categories (mania, melancholia, monomania, dementia, general paralysis of the insane, epilepsy, toxic insanity, and congenital mental deficiency); they rejected only moral insanity.

The intellectual and scientific constraints that inhibited the development of psychiatric nosology persisted for much of the nineteenth century. When, toward the close of his long career, the venerable Pliny Earle was approached by Bell in 1886 about the possibility of developing a universally accepted classification of mental diseases, Earle (16) responded in somewhat negative terms. "In the present state of our knowledge," he wrote, "no classification of insanity can be erected upon a pathological basis, for the simple reason that, with but slight exceptions, the pathology of the disease is unknown. . . . Hence, for the most apparent, the most clearly defined, and the best understood foundation for a nosological scheme for insanity, we are forced to fall back upon the symptoms of the disease—*the apparent mental condition,* as judged from the outward manifestations." The oldest, simplest, and most practical classification systems (mania, monomania, dementia, and idiocy), therefore, were still of considerable value.

Recognition of the difficulties that blocked the formulation of a nosology of insanity did not in any way inhibit etiological discussions. To be sure, psychiatrists were aware of their inability to demonstrate meaningful relationships between causal elements and the presence of particular behavioral signs or symptoms. Yet the social and cultural roles of medicine required that all physicians—psychiatrists and others—provide some explanation of disease processes. This was as true for the early part of the nineteenth century as it was for the closing decades, when a new ideal of scientific medicine (symbolized by the introduction of antisepsis in the 1870s and pathogenic specificity in the 1880s) was taking shape.

Nineteenth-century psychiatric etiological concepts reflected broad social perceptions and prevailing cultural norms. Consequently, etiological discussions tended to be protean and nonspecific in character. Insanity, observed Walter Channing (17), involved an internal relationship between the individual and the environment that remained a mystery. Given the immense complexities in understanding the inner life history of a person, he emphasized external predisposing causes. Mental illnesses followed several conditions: the harmful effects of the increasing demands of modern civilization, the migration from abroad of individuals already well on the road to degeneracy, and the role of such factors as marriage and occupation. Nor were Channing's etiological theories unique; virtually every psychiatrist focused on external elements. The list seemed endless: addiction to alcohol, drugs, and tobacco; sexual excesses; improper nutrition; inadequate housing; misdirected education; uterine and ovarian diseases; and moral or psychological causes such as domestic difficulties, grief, anxiety, adverse circumstances, business failure, financial difficulties, sudden fright, worry, and mental overwork (18–21).

For much of the nineteenth century mental illnesses were loosely classified on the basis of symptoms with unprovable etiology or content. Toward the close of the century, however, interest in psychiatric nosology reawakened. Psychiatrists began to shift their attention to the course and outcome of mental illnesses. Emil Kraepelin (22) in particular singled out groups of signs as evidencing specific disease entities such as dementia praecox and, later, manic-depressive psychosis. Studying thousands of patients at his clinic in Heidelberg, Kraepelin identified the disease entity in terms of its eventual outcome. Dealing with a large mass of data, he sorted out everything that individuals had in common, omitting what he regarded as purely personal data. In this respect he diverted attention away from the unique circumstances of individuals toward more general and presumably universal disease entities. In so doing, he was simply emulating a distinct trend in medical thinking in general.

The Kraepelinian emphasis on classification was not immediately accepted; nosological uncertainty persisted. In 1894 the Committee on Statistical Tables (23) reported that many members regretted the fact that the American Medico-Psychological Association (now APA) lacked a nosology that "would place its members upon common ground." Six years later, Henry J. Berkley (24), Clinical Professor of Psychiatry at Johns Hopkins, noted that a classification based on clinical symptoms was unsatisfactory "because the indications of one form of disease frequently overlap those of another." Similarly, an etiological nosology was defective "inasmuch as the fundamental causation is frequently unknown and unascertainable." Berkley fell back on a classification based on morbid anatomy, "for when the pathology of a disease has been once recognized, the course can be predicted with some certainty, and the treatment instituted rests upon a solid foundation." In another textbook published in 1905, Stewart Paton (25) conceded that classification in psychiatry and medicine differed; the former did not deal with "definite disease entities, such as typhoid fever or pneumonia," where a demonstrable causal link was present. Nor had psychiatrists been able to establish a connection between lesions and behavior. The only rational method, Paton suggested, was one that took into consideration "all the possible facts bearing upon the case." His preferred nosology was a system that divided diseases into the "defect psychoses—idiocy, imbecility, and other degrees of mental debility," psychoses due to autointoxication (admittedly unproven), and the groups of manic-depressive insanity and dementia praecox. The growing preoccupation with classification led Charles G. Hill (26) in his presidential address before the American Medico-Psychological Association in 1907 to observe that there was little room for addition "unless we add 'the classifying mania of medical authors.' "

SOCIAL SCIENCES AND THE FEDERAL CENSUS

The impetus to create a psychiatric nosology came largely from outside of psychiatry or medicine. By the end of the nineteenth century a number of new social science disciplines had come into existence. Many of the individuals associated with these new disciplines were concerned not only with developing a scientific understanding of individual and social behavior but also with applying this understanding to a series of pressing social problems that seemed to threaten the very fabric of society.

In its quest for empirical data, social science drew upon the tradition of statistical analysis that had emerged during the first half of the nineteenth century. Ultimately, a general consensus developed around the indispensable utility of the federal census. To those hoping to interpret individual and collective behavior in scientific terms, the census was not merely an undertaking designed to collect data. On the contrary, the census represented a radical faith that quantitative research, when merged with administrative rationality, could replace politics. Statistical knowledge could thus serve as the foundation for social policy and end the pernicious bickering over theory, principles, and politics.

As early as the 1830s, concern with morbidity, mortality, and dependency had stimulated efforts to gather statistical data that could presumably illuminate their causes and thus assist in the development of appropriate policies. The federal census of 1840, for example, attempted to enumerate the insane, but with little success. The obstacles confronting the collection of aggregate data were formidable, and administrative mechanisms were weak or nonexistent (27, 28). The major turning point came with the tenth census in 1880. The scope of this census was evident in its size; it ran to 25 volumes plus a three-volume compendium (compared with two volumes in 1870). More importantly, dependency was the subject of an entirely separate volume prepared under the supervision of Frederick H. Wines, who was already a significant figure in American welfare. Wines had been appointed as secretary of the Illinois Board of State Commissioners of Public Charities in 1869 and subsequently became prominent in the National Conference of Charities and Corrections. His stature was such that his views on the care and treatment of a variety of dependent groups, including the mentally ill, the mentally retarded, and imprisoned criminals, received national attention.

Wines's 581-page volume was published in 1888 under the title *Report on the Defective, Dependent, and Delinquent Classes . . . as Returned at the Tenth Census (June 1, 1880)* (29). That Wines regarded the census as an instrument of policy was indisputable. In his eyes the organization of modern society was intimately related to the increase in dependency, a development he viewed with considerable misgivings. "There is a morphology of evil which requires to be studied," he wrote. "For the information of legislatures it is important that the whole extent of the evil to be contended against shall be known, and that it shall be accessible in a single report, in order that they may make adequate provision for its care or alleviation" (p. x). Wines's analysis went beyond mere aggregation of data pertaining to insanity; he began to speculate on the relationship between mental illness and such variables as sex, nativity, race, geographical residence, age, and marital status.

Wines was cognizant that psychiatrists had been unable to agree on a satisfactory nosology. He called attention to the fact that existing nosologies represented a melange of etiology, symptomatology, and description. Some classifications were "based upon symptoms" and some upon "physical causes"; others were "a mixture of the two"; and still others took into account "the complications of insanity." After consulting with a series of alienists, Wines decided to identify seven forms of insanity: mania, melancholia, monomania, paresis (general paralysis of the insane), dementia, dipsomania, and epilepsy (29, p. xli). A decade later, Dr. John Shaw Billings (30), the physician who created what is today the National Library of Medicine, served as president of the American Public Health Association, and prepared the eleventh census volume dealing with dependency, which followed Wines's classification but subdivided mania and melancholia into acute and chronic.

After 1900, the Bureau of the Census expanded its coverage of dependent groups in general and the mentally ill in particular. In 1904 and 1910 it conducted two special censuses dealing with the institutionalized insane. The first focused attention on the ethnic and racial characteristics of the institutionalized mentally ill and did not use any psychiatric nosological categories because of the absence of a standard classification. The census officials' preoccupation with race and ethnicity was related to the growing fear that the alleged racial superiority of the native-born population, whose families were originally from Western and Northern Europe, was being threatened by large-scale immigration of presumably inferior groups from Eastern and

Southern Europe. Eugenical concepts, which posited a relationship between race and culture, enjoyed considerable popularity at the turn of the century. A number of states passed laws regulating marriage for eugenical purposes, mandating the segregation of the feebleminded and providing for the involuntary sterilization of some of the retarded and mentally ill (31–33). Although the data collected in 1904 provided relatively little support for the validity of eugenical concepts, it was evident that the categories used by the Bureau of the Census (34) reflected some of the concerns about the relationship between race and immigration on the one hand and social problems and dependency on the other.

The special census of 1910 was even broader in scope than its predecessor 6 years before and reflected a growing sophistication in the analysis of statistical data. Once again the focus was on the role of demographic characteristics and the relationship between insanity and social factors. With the exception of some brief data on the admission of patients with alcoholic psychosis and paresis (two fairly well-recognized categories) and death rates of those suffering from mental disorders, the census again all but ignored psychiatric nosology. That the compilation reflected the growing importance of the social sciences was evident. Responsibility for its preparation lay with Joseph A. Hill (35), who had received his doctorate in Germany and taught political economy at Harvard before joining the Bureau of the Census in 1898. Hill offered little comfort to those fearful of the new immigration. The claim that insanity was increasing rapidly, he wrote, was dubious. A variety of determinants shaped the statistics of insanity: the growing practice of institutionalizing the insane, the increasing average length of life, new diagnostic methods in psychiatry leading to the detection of mental factors in physical illness, the establishment of dispensaries, provision for "voluntary" and emergency commitment, and better modes of transportation (such as automobiles) that made it possible to bring individuals in poor physical condition to mental hospitals. By correcting for the age distribution of the entire native and foreign-born population, Hill also demonstrated that the allegation that immigrants had higher rates of mental illnesses was in error. "The age difference," he wrote, "probably goes further than any other factor toward explaining the contrast between the native white and the foreign-born in respect to the proportionate numbers admitted to hospitals for the insane." Other differences between the two groups might also be accounted for by sex distribution or residence in urban or rural areas.

STATISTICS AND EPIDEMIOLOGY

The growing involvement of the Bureau of the Census with the statistics of mental illnesses was indicative of the concern outside of psychiatry with policy implications and future trends. The presumption was that demographic data dealing with the institutionalized mentally ill would be useful to public officials responsible for administering large hospital systems. Preoccupation with public policy, however, reinforced the lack of attention given to the imprecise nature of diagnostic categories—an oversight that contradicted generally accepted epidemiologic principles.

Psychiatrists initially manifested relatively little interest in the activities of the Bureau of the Census. This began to change as concern regarding mental hygiene and prevention mounted. When Dr. Thomas W. Salmon became medical director of the recently founded National Committee for Mental Hygiene in 1912, it was clear that the preoccupation with mental hygiene transcended concern with the problems of the institutionalized insane. Indeed, Salmon had a new and radical vision of the role of psychiatry. In the past, he observed in 1917 (36), the isolation of patients in mental hospitals had also isolated psychiatrists. A new kind of psychiatry, on the other hand, would reach beyond hospital confines and play a crucial part "in the great movements for social betterment." He urged his colleagues to undertake research, to help shape public policy, to lay the foundations of mental hygiene, to supervise the care of the retarded, to promote eugenical practices, to control alcoholism, to manage abnormal children, to define the treatment of criminals, and to play crucial roles in the prevention of crime, prostitution, and dependency.

Even if not universally accepted by the specialty, such broad goals helped to move psychiatrists into the community and involve themselves in a broad range of problems not related specifically to the needs of severely mentally ill individuals traditionally found in hospitals. Out of these experiences came a new psychiatric interest in statistics and epidemiology. As early as 1908 the Bureau of the Census had asked the American Medico-Psychological Association to appoint a Committee on Nomenclature of Diseases to facilitate the collection of data (37). In subsequent years the interest of census officials in a standard psychiatric nosology grew even stronger. The Association finally created a Committee on Statistics in 1913. Its members quickly affirmed the need to develop a uniform system to gather data on mental diseases and mental hospitals. In 1917 (38) they reported that the lack of uniformity "makes it absolutely impossible at the present time to collect comparative statistics concerning mental diseases in different states and countries, and extremely difficult to secure comparative data relative to movement of patients, administration, and cost of maintenance and additions." Such data, if collected in a uniform and systematic manner, "would serve as the basis for constructive work in raising the standard of care of the insane, as a guide for preventive effort, and as an aid to the progress of psychiatry." They added, "The present condition with respect to the classification of mental diseases is chaotic. This condition of affairs discredits the science of psychiatry and reflects unfavorably upon our Association."

Cognizant that the Bureau of the Census would continue to expand its data-gathering activities, the members of the Committee on Statistics urged their colleagues to prepare a uniform nomenclature of mental diseases. The Association, with the cooperation of the National Committee for Mental Hygiene, issued the first standardized psychiatric nosology, *Statistical Manual for the Use of Institutions for the Insane* (39) in 1918. This manual divided mental disorders into 22 principal groups. One of these represented undiagnosed psychoses, one represented patients without psychoses, and the remaining 20 categories rested for the most part on the belief that mental disorders had a biological foundation. These categories were traumatic psychoses, senile psychoses, psychoses with cerebral arteriosclerosis, general paralysis, psychoses with cerebral syphilis, psychoses with Huntington's chorea, psychoses with brain tumor, psychoses with other brain or nervous diseases, alcoholic psychoses, psychoses due to drugs and other exogenous toxins, psychoses with pellagra, psychoses with other somatic diseases, manic-depressive psychoses, involution melancholia, dementia praecox (subsequently schizophrenia), paranoia or paranoid conditions, epileptic psychoses, psychoneuroses and neuroses, psychoses with constitutional psychopathic inferiority, and psychoses with mental deficiency.

That American psychiatrists preferred a somatic nosology was hardly surprising. In 1918 the overwhelming majority of those who were identified with psychiatry were employed in mental hospitals; the number in noninstitutional settings was negligible. In public hospitals psychiatrists dealt with patients with severe physical impairments. In 1922, for example, 33.4% of all first admissions represented psychoses of known somatic origins; by 1940 the figure had risen to 42.4%. (The data for this paragraph are taken from the U.S. Bureau of the Census annual compilations of hospital statistics from 1926 to 1946. The first volume was published in 1926 [40].) If we assume that a substantial proportion of individuals in the functional categories also suffered from conditions with a somatic origin—an assumption that may be warranted from present-day data—it is evident that mental hospitals provided care for a patient population with severe physical as well as mental problems. The fact that the somatic group had a higher death rate than the group with functional psychoses suggests that the diagnoses were not inaccurate. In 1940 the somatic group accounted for 19,357 deaths (61.6%) out of a total of 31,417. The somatic nosology adopted in 1918, therefore, mirrored in part the nature of psychiatric practice.

From the point of view of the Bureau of the Census, the adoption of a formal classification system was of major importance. Indeed, in 1920 the Bureau published its own nomenclature of diseases (41), which relied on the *Statistical Manual* (39) in defining psychiatric categories. It conceded its inability to draw a clear line between symptoms and diseases and admitted that many terms used to describe pathological conditions might in the future be regarded as symptoms if the etiology of the disease were discovered. Nevertheless, the collection of statistical data required a formal nomenclature. Three years after the publication of its own nosology, the Bureau of the Census began its annual collection of the statistics of the institutionalized mentally ill population (40), which was continued after World War II by the National Institute of Mental Health (NIMH).

The adoption of a uniform psychiatric nosology was not without controversy. The major opponent was Adolf Meyer. Meyer's genetic-dynamic psychiatry attempted to integrate the life experiences of the individual with physiological and biological data. Training several generations of American psychiatrists at Johns Hopkins between 1910 and 1941, Meyer had never been fond of Kraepelinian nosological psychiatry, given his belief that the life history of the individual was the most important element in the etiology of mental disorders. He therefore refused to be identified with the nosology that was prepared by the Committee on Statistics, of which he was a member. The difference, he wrote to E.E. Southard (42, 43), is "that I have no use for the essentially 'one person, one disease' view; that I prefer to speak of an individual *presenting* certain facts that we can do something with in the way of definite demonstration, and, if possible, in the way of some prediction of a type of lesion, and along the lines of attack in the way of some therapeutic activity, and also along the lines of prognosis. Whether a person has a dozen such facts or only one, is to be a matter of demonstration and not of legislation" (42). Meyer told Samuel T. Orton (44, 45) that "statistics will be most valuable if they do not attempt to solve all the problems of administration and psychiatry and sociology under one confused effort of a one-word diagnosis marking the individual. . . . The statistics published annually as they are now are a dead loss to the States that pay for them, and an annual ceremony misdirecting the interests of the staff." Orton (46) was equally critical. The Association's classification, he insisted, was deficient on three counts. First, it was "too narrow in that it excludes all disorders of the nervous system, which do not produce . . . psychoses." Second, it was "illogical" because the categories were based in part on etiology, in part on pathology, and in part on purely clinical data. Third, it was "inconsistent."

Despite such criticisms, the *Statistical Manual* became the definitive nosology of the interwar years and went through no fewer than ten editions between 1918 and 1942. The first seven editions incorporated minor changes; the latter three included more extensive modifications. The tenth edition (47) continued to emphasize the biological basis of most mental disorders but made provision for the psychoneuroses (hysteria, compulsive states, neurasthenia, hypochondriasis, reactive depression, anxiety state, anorexia nervosa, and mixed psychoneuroses) and primary behavior disorders (adult maladjustment and primary behavior disorders in children). As late as 1940, the somatic viewpoint continued to shape psychiatric nosology.

Paradoxically, the classification system incorporated in the *Statistical Manual* was only of marginal concern to psychiatrists and their patients. Its categories were quite general, for the goal was to facilitate the collection of institutional data rather than to provide definitive diagnoses that in turn were related to specific therapies. Psychiatric therapies between the two World Wars, as a matter of fact, were for the most part eclectic and nonspecific; diagnosis was of only marginal significance.

AFTER WORLD WAR II: PSYCHODYNAMICS AND SOCIAL ACTIVISM

World War II marked a major watershed in the history of the care and treatment of the mentally ill in the United States. Many psychiatrists who served in the military came to some novel conclusions. They found that neuropsychiatric disorders were a more serious problem than had previously been recognized, that environmental stress associated with combat contributed to mental maladjustment, and that early and purposeful treatment in noninstitutional settings produced favorable outcomes. These beliefs became the basis for claims after 1945 that early identification of symptoms and treatment in community settings could prevent the onset of more serious mental illnesses and thus obviate the need for prolonged institutionalization. The war reshaped psychiatry by attracting into the specialty a substantial number of younger physicians whose outlook, molded by their wartime experiences, was based on psychodynamic and psychoanalytic concepts. After 1945 many of these psychiatrists assumed leadership positions within the specialty, fought to reorganize APA (48), and attempted to forge new policies that broke with the traditional consensus on the need for prolonged hospitalization of mentally ill individuals.

To be sure, the foundation of psychodynamic and psychoanalytic psychiatry had its origins in the early part of the twentieth century. Nevertheless, its triumph within the specialty had to await the transforming experiences of World War II. During that conflict, psychiatrists made major contributions in developing simple but effective means of dealing with large numbers of neuropsychiatric casualties. They found that supportive forms of psychotherapy, when combined with rest, sleep, and food, produced almost instantaneous results. Treatment in a local setting also ensured that soldiers were not separated for any length of time from their units and established social relationships. Overall, about 60% of the soldiers who became neuropsychiatric casualties were returned to duty within 2–5 days. The highest success rates were found in forward combat units; the lowest at rear-echelon hospitals. More than any other element, the success in returning to active duty servicemen who experienced psychological problems renewed a spirit of therapeutic optimism and activism, which was carried back into civilian life after the war (49–52). "Our experiences with therapy in war neuroses have left us with an optimistic attitude," Roy R. Grinker and John P. Spiegel (53) reported in a chapter for a manual of military psychiatry. "The lessons we have learned in the combat zone can well be applied in rehabilitation at home."

World War II had other effects as well. In 1941, the status of psychiatrists in military as well as civilian life was marginal. Only 35 members of the Army Medical Corps were assigned to neuropsychiatric sections in hospitals. During the war, psychiatrists slowly increased their presence and importance. At the beginning of 1944 the specialty was raised to the level of a division within the Office of the Surgeon General and placed on an equal organizational level with medicine and surgery. William C. Menninger, who directed the division, was the first psychiatrist to be elevated to the rank of brigadier general. By the end of the war about 2,400 physicians had been assigned to psychiatry, although perhaps less than a third had previous training in the specialty (54, 55). In 1940, by way of comparison, APA had a total membership of only 2,295. The war, in other words, brought into psychiatry hundreds of physicians who might otherwise have selected different medical specialties. Their wartime experiences in successfully treating neurotic symptoms in noninstitutional settings (and allegedly preventing the onset of more serious psychotic symptoms) reinforced the growing importance of a psychodynamic and psychoanalytic model that ultimately became the basis for the postwar transformation of the specialty. More than anything else, the war helped to unify the belief that environmental stress contributed to mental maladjustment and that purposeful human interventions could alter psychological outcomes.

In the postwar era, the traditional preoccupation with the severely mentally ill in public mental hospitals slowly gave way to a concern with the psychological problems of a far larger and more diverse population as well as social problems generally. Persuaded that there was a continuum from mental health to mental illness, psychiatrists increasingly shifted their activities away from the psychoses toward the other end of the spectrum in the hope that early treatment of functional but troubled individuals would ultimately diminish the incidence of the more serious mental illnesses.

Nowhere was the changing outlook of American psychiatry better revealed than in the formation of the Group for the Advancement of Psychiatry (GAP) in 1946. GAP represented a group of "young Turks" determined to reshape APA. Two years before the formation of GAP, the APA Council had authorized its president to appoint a Special Committee on Reorganization to recommend the employment of a medical director for APA and to study the organization's structure (56–58). Fearful that the heterogeneity of the Association might preclude decisive action, William C. Menninger and a group of colleagues met at the APA meetings in May 1946 to found GAP. There was general agreement that GAP would operate as a pressure group within APA to overcome the apathy of its leaders and, in particular, its "incapacity to function." The new organization was based on the presumption that psychiatry's responsibilities and functions transcended institutional care and treatment of the mentally ill (59–61). "I do feel," Menninger (60) told a colleague in early 1947, "that American psychiatry needs renovation in the sense of consideration of social problems and social needs."

Indeed, the early reports of GAP (issued in final form as published documents) reveal a willingness to engage in a debate on broad social and political issues that bore little direct relationship to the problems of the institutionalized mentally ill. A draft report on the social responsibility of psychiatry (62) urged that psychiatric insights be used in the service of social action (defined as "a conscious and deliberate wish to change society"). Preventive psychiatry, therefore, had to move "out of the hospitals and clinics and into the community" (63). Although GAP's social activism and emphasis on a psychodynamic social psychiatry quickly aroused hostility within the specialty, in a short time the ideological orientation of GAP prevailed, and its views were shared by the majority of APA members.

In emphasizing the need to focus on nonpsychotic but presumably troubled individuals, psychodynamic psychiatrists tended to blur nosological categories. The changing character of the specialty was reflected in its terminology. Traditionally, diagnoses were expressed in the language of pathology; the presumption was that changes in behavior, which admittedly might be related to environmental factors, had a biological foundation. Postwar psychiatrists, by way of comparison, did not necessarily reject traditional formulations. Their interest in the nature of personality (normal as well as abnormal), the role of childhood and the influence of parenthood, and the ability of the organism to adjust to the environment in ways that were both effective and satisfying, however, led them to use a quite different terminology. Their new language emphasized the need to assist unhappy and neurotic individuals, presumably through different psychotherapies. In emphasizing their ability to deal with such varied concerns as parent-child relationships, marriage, emotional maturity, and occupational roles, the specialty appealed to a broad public eager for assistance in dealing with the problems of ordinary life (64–66).

THE NEW PSYCHIATRIC NOSOLOGY

Nowhere was the change in the nature of postwar psychiatry better illustrated than in the effort to create a new psychiatric nosology. During the 1940s, discontent mounted with the classification system prepared more than two decades earlier. Military and Veterans Administration psychiatrists found themselves using a nomenclature ill-adapted for 90% of their patients. Minor personality disturbances—many of which were of importance only because they occurred within a military context—were placed in the "psychopathic personality" category. The "psychoneurotic" label was given to men who had developed symptoms because of the stress of combat. There was virtually no recognition of psychosomatic disorders. Indeed, by the end of the war the Army and Navy had adopted their own classifications, which subsequently became the basis for revisions of the *International Statistical Classification* (*DSM-I*, pp. v–viii).

The nosological confusion, proliferation of nomenclatures, and shift toward psychodynamic and psychoanalytic concepts led the APA Committee on Nomenclature and Statistics in 1948 to postpone further changes in its manual and solicit instead suggestions for change (67). By 1950 it had prepared mimeographed copies of a revised psychiatric nosology, which was widely circulated to various individuals and organizations; a completed version was presented to the APA Council in 1950 for its approval (*DSM-I*, pp. vii–x). In 1952 APA formally published *DSM-I* (68).

DSM-I reflected the intellectual, cultural, and social forces that had transformed psychiatry during and after World War II. It divided mental disorders into two major groupings. The first represented cases in which the disturbed mental function resulted from or was precipitated by a primary impairment of brain function. Such brain syndromes were associated with a variety of somatic conditions—infection; drug, poison, or alcoholic intoxication; trauma; circulatory or metabolic disturbances; intercranial neoplasms; multiple sclerosis; and Huntington's chorea or other diseases of hereditary origin. The second category encompassed disorders resulting from a more general inability of the individual to adjust, in which brain function disturbance was secondary to the psychiatric illness. *DSM-I* (pp. 9–43) divided this group into psychotic and psychoneurotic disorders. The former included manic-depressive and paranoid reactions as well as schizophrenia. The latter, in turn, was composed of anxiety, dissociative, conversion, phobic, obsessive-compulsive, and depressive disorders as well as a variety of personality disorders that included emotional instability, compulsiveness, antisocial behavior, sexual deviation, alcoholism, drug addiction, stress, and various reactions associated with different age categories.

The prominence of psychodynamic and psychoanalytic concepts in *DSM-I* mirrored fundamental changes within psychiatry. The pressure for change, as a matter of fact, was generated largely by analytically oriented psychiatrists who had few ties with public mental hospitals; most of them were in medical schools, clinics, and private practice. By 1956, for example, only about 17% of the 10,000 or so members of APA were employed in hospitals, compared with more than two-thirds in 1940. (Data for 1956 are based on a 10% subgroup [N=943] of the 10,000 members of APA, according to the *Biographical Directory* for 1957

[69].) The clientele of psychiatrists not affiliated with public mental hospitals tended to come from (to use *DSM-I* categories) the ranks of the psychoneurotic, many of whom seemed to benefit from psychotherapy. Psychodynamic psychiatrists also were more committed to social activism, a commitment mirrored in the activities of GAP.

The growing dominance of psychodynamic and psychoanalytic concepts was reflected in changes in medical and postgraduate education. After 1945 the number of psychodynamic and psychoanalytic psychiatrists affiliated with medical schools increased rapidly. The result was predictable: more and more psychiatry was taught in all 4 years, thus serving as a means of introducing and recruiting young medical students to the specialty. At the same time, psychiatric teaching influenced other departments. NIMH grants, in turn, subsidized both undergraduate and residency training (70, 71), and the number of psychiatric residencies expanded rapidly. In 1946 there were 155 residency programs; a decade later the total reached 294. The number of actual residencies in this period leaped from 758 to 2,983. The rising prestige and attractiveness of psychiatry was accompanied by a dramatic increase in the proportion of medical school graduates selecting the specialty, which in 1954 peaked at 12.5% (72, 73).

Even more important than the increase in actual numbers was the shift in orientation that marked undergraduate and graduate (i.e., residency) training. A 1942 report on psychiatric education by Franklin G. Ebaugh and Charles A. Rymer (74) had reflected the influence of Meyer. Transitional in character, their work began with the observation that the dominance of the organic point of view in medical education prevented "the proper recognition of the place of psychiatry in the medical curriculum." The concept of organic disease was so pervasive that "functional components are difficult to grasp and appear in the nature of improbability." Other elements contributed to the denigration of psychiatry: a moralistic view of mental disorders, the emotional reaction of medical students to psychiatric concepts, and the seeming hopelessness of mental conditions. Desirable changes, Ebaugh and Rymer concluded, had to rest on three fundamental principles: the concept of man as a whole, the adoption of "a genetic-dynamic concept of mental disorders," and the inseparable relationship of psychiatry and medicine (mediated by the psychosomatic approach) with a recognition of the "emotional factors in disease."

After 1945, by way of contrast, American psychiatry to an unprecedented degree was shaped by psychoanalytic theory, which emphasized the psychological mechanisms that mediated between instinctual biological drives and the pressures of the external environment. Change was already evident by the end of the war. In 1946 the American Board of Psychiatry and Neurology gave its stamp of approval to psychodynamic principles; this anticipated the emergence of a more psychoanalytically oriented psychiatry. Training in the specialty, the Board announced, had to include clinical work with psychoneurotic and psychotic patients (75, 76). Clinical experience had to be integrated "with the study of the basic psychiatric sciences, medical and social psychology, psychopathology, psychotherapy, and the physiological therapies" (75). Psychiatrists had to be taught to collaborate with social workers, clinical psychologists, courts, and other social agencies. Finally, residents had to be exposed to neurology to enable them "to recognize and to evaluate the evidences of organic neurological disease" (75).

In 1951 and 1952 APA and the Association of American Medical Colleges sponsored two important conferences. The first (77) dealt with psychiatry in medical education and the second (75) with residency training. Both were dominated by the psychodynamic perspective. Anxious to alter the marginal role of the specialty, the participants at the first conference urged that all medical students be exposed to psychiatric insights in each of the 4 years. The basic aim was "to equip the student with a reasonably adequate knowledge of the facts of human nature" (77). More specifically, all medical students had to have the ability "to diagnose correctly the condition of patients who are emotionally disturbed and who may be expressing their distress in physical, psychological or social symptoms. This ability implies . . . a reasonable understanding of the zones of healthy and sick behavior in our society and, more particularly, the ability to differentiate between normal, neurotic, psychopathic, psychotic, and intellectually defective behavior" (77).

The deliberations at these conferences subsequently led to the preparation of a statement by the APA Committee on Medical Education (77–79). It defined the minimum that all physicians should know about psychiatry and the means by which medical schools could teach such knowledge and skills to their students. The committee recommended that during the first 2 years all medical students be exposed to theories of personality growth, development, structure, and integration; adaptive needs; social and cultural forces affecting personality and behavior; the role of language and mentation; the part played by emotions in physiological functioning; and psychopathology. The curriculum should not attempt to train physicians to become psychiatrists but, rather, to develop "well-rounded physicians, who, in their relationships with all patients, recognize the importance of unconscious motivation, the role of emotional maladjustment in the etiology and chronicity of illness, the emotional and personality problems engendered by various illnesses; and who habitually see the patient in his family and general environmental setting" (78).

That psychodynamic insights quickly dominated the teaching of psychiatry in medical schools was apparent from a GAP survey in 1959–1960 (80). Out of 93 U.S. and Canadian institutions, 88 taught psychodynamics, 87 taught personality growth and development, and 77 taught psychotherapy and clinical syndromes. The number of hours in the curriculum devoted to psychiatry also quadrupled between 1940 and 1960. Virtually every chairperson of a department of psychiatry stated unequivocally that the psychodynamic frame of reference (as contrasted with the descriptive or organic) was dominant.

The publication of *DSM-I* in 1952, therefore, was a visible symbol of the transformation of American psychiatry. Unlike the *Statistical Manual, DSM-I* elevated the significance of diagnosis. In presenting the new nosology, George N. Raines (68), chairperson of the APA Committee on Nomenclature and Statistics responsible for its publication, observed that "accurate diagnosis is the keystone of appropriate treatment and competent prognosis." He was critical of the claim that individual differences precluded the use of standardized categories. "Sound diagnosis," he added, "is possible only with a nomenclature in keeping with current concepts of psychiatric illness." *DSM-I,* moreover, was "sufficiently flexible and inclusive to permit the introduction of new and original ideas."

CONCLUSIONS

Nosologies—psychiatric or otherwise—are rarely etched permanently in stone. *DSM-I,* like its predecessor and successors, grew out of a specific historical context and reflected the dominance of psychodynamic and psychoanalytic concepts. The shift toward a more biological orientation during and after the 1960s would become the occasion for renewed nosological debate and the creation of new categories.

To contemporary psychiatrists the history of nosology represents a version of the idea of progress; advances in knowledge supposedly lay the foundation for the creation of new categories that describe reality in better and more accurate terms. Within such a perspective, the history of psychiatry is moving on an upward gradient toward an ideal end. In this specific instance, the final goal is a definitive and presumably unchanging nosology of mental illnesses. To more skeptically minded historians, however, the only constant is the process of change itself. The search for a definitive nosology, therefore, may simply be an expression of the perennial human yearning for omniscience—an attribute eagerly sought by many but never yet found.

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Subtyping *DSM-III-R* Primary Insomnia: A Literature Review by the DSM-IV Work Group on Sleep Disorders

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Objective: The authors review the usefulness, reliability, and validity of recently proposed subtypes of primary insomnia. DSM-III *uses "primary insomnia" to indicate chronic insomnia not associated with other diagnosable mental or medical disorders, whereas the* International Classification of Sleep Disorders (ICSD) *recognizes three subtypes: psychophysiological insomnia, idiopathic insomnia, and sleep state misperception. Method: After reviewing all of the primary source references for each insomnia disorder in the* ICSD *and all of the additional primary sources cited in each of these, the authors conducted an automated literature search using Medline. Of the 48 primary sources located, the authors selected 27 studies that were reported in peer-reviewed journals, had the largest available subject groups, used diagnostic reliability procedures, and included control groups. Results: The studies reviewed contained limited empirical support for the proposed distinction between idiopathic and psychophysiological insomnia. Sleep state misperception appears, however, to be a highly prevalent feature of chronic insomnia generally, rather than only a specific disorder per se. Conclusions: The authors conclude that there is not yet sufficient empirical evidence to warrant the abandonment of* DSM-III-R *"primary insomnia" and the adoption of the* ICSD *subtypes in* DSM-IV. *However, they affirm the heuristic value of the* ICSD *subtypes and the need for field trials to compare the performance characteristics of the* DSM-III-R *and* ICSD *systems with respect to 1) interrater reliability, 2) effects of rater expertise (generalist versus specialist) on rates of agreement, and 3) effects of polysomnographic data on rates of agreement.*

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The classification of sleep/wake disorders, particularly those involving persistent insomnia, has developed to a point similar to the classification of depressive disorders 20 years ago. While there are several competing nosologies, basic work defining the reliability and validity of the proposed systems has not been performed. Not surprisingly, since competing claims are based on appeals more to opinion than to data, we have witnessed considerable controversy in the field, particularly since the publication of *DSM-III-R* in 1987. The controversy revolves around three major issues: 1) the extent to which sleep disorders, particularly those involving insomnia, can be classified into subtypes, 2) the feasibility and utility of more differentiated versus general classifications in the practice of psychiatry, and 3) the value and place of sleep laboratory data in the differential diagnosis of insomnia complaints.

DSM-III-R uses the term "primary insomnia" to indicate insomnia that lasts longer than 1 month and is not related to other diagnosable medical or psychiatric disorders. This has caused controversy among psychiatric sleep researchers and clinicians, some of whom have objected that the term is difficult to interpret and groups together patients with widely differing complaints of insomnia.

In reviewing the *DSM-III-R* diagnostic categories for inclusion and/or revision in *DSM-IV*, the work group on sleep disorders decided to use the recently

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published *International Classification of Sleep Disorders* (*ICSD*) (1) as a template for conducting a literature search. In this context, primary insomnia would include the three subtypes of "intrinsic" insomnia (i.e., presumably due to factors arising within the patient) in the *ICSD*: psychophysiological insomnia, sleep state misperception, and idiopathic insomnia. Accordingly, we reviewed the research literature on the frequency and validity of psychophysiological insomnia, sleep state misperception, and idiopathic insomnia. In addition, we reviewed the research literature relating to the seven "extrinsic" types of insomnia (i.e., presumably due to factors arising outside the patient) in the *ICSD*: inadequate sleep hygiene, environmental sleep disorder, altitude insomnia, adjustment sleep disorder, insufficient sleep syndrome, limit-setting sleep disorder, and sleep-onset association disorder. As will be suggested, most insomniac patients appear to show an interaction of intrinsic and extrinsic factors. Hence, we chose to include both groups in our review of primary insomnia.

The critical issue is whether subtyping primary insomnia enhances communication, clinical utility, and/or validity of the diagnostic process. A related, and equally important, issue is whether the *ICSD* subgroups of primary insomnia are clinically relevant to the practice of psychiatry and can be used reliably by psychiatrists. For example, do the *ICSD* subgroups of primary insomnia denote clinical conditions that have developed in response to distinct etiologic factors? Do they predict a differential response to specific therapeutic interventions? Is a different family history of sleep disorders associated with each? In asking whether there is empirical support for the *ICSD* subtypes of primary insomnia, as well as for the *ICSD* subtypes of extrinsic insomnia, it is important to remember that clinical constructs, such as those proposed by the *ICSD*, may have considerable heuristic value and, as such, may drive clinical investigation in psychiatric sleep research and sleep disorders medicine.

As noted by Hauri (2), the 1979 Association of Sleep Disorders Centers' *Diagnostic Classification of Sleep and Arousal Disorders* (*ASDC*) (3) and its successor, *ICSD* (1), are both based on extensive clinical experience and appear to represent the consensus of most active sleep research clinicians in psychiatry. When one contrasts the classification of insomnia in *DSM-III-R* with the classification in the *ASDC* and *ICSD*, the critical issue is to determine the number of groups, or "clusters," of patients with insomnia not related to diagnosable medical or psychiatric disorders ("primary insomnia"). Hauri (2) has stated the issue and the dilemma well: "With too few clusters, interpretation is difficult because many widely differing patients are lumped together. With too many clusters, interpretation is also difficult, because some of the differences between clusters become minute and esoteric." Accordingly, it would appear desirable for the *DSM-IV* nosology of sleep/wake disorders to achieve a position between the two extremes.

The resolution of these issues must depend primarily on published empirical support for the *ICSD* clinical subtypes of primary insomnia. A related key question is whether factors perceived to be clinically important in the pathogenesis and exacerbation of insomnia should be elevated to clinical subtypes at this time, on the basis of published data. Finally, we must begin to address the relative performance characteristics and the clinical/research utility of the *DSM-III-R* and *ICSD* classifications of insomnia disorders.

METHOD

We reviewed all of the primary source references in the bibliography for each insomnia disorder in the *ICSD*. We then pursued all the additional primary sources cited in each of these referenced papers. Our third step was to conduct an automated literature search using Medline. We found a total of 48 primary sources published over the last two decades in the English-language literature. Each of these 48 reports was then coded according to the following eight criteria: 1) type of publication (i.e., peer-reviewed, research abstract, or review), 2) number of subjects, 3) use of specific diagnostic criteria (e.g., *ASDC*, *DSM-III-R*, or Research Diagnostic Criteria), 4) use of diagnostic reliability procedures, 5) inclusion of control or contrast groups, 6) inclusion of follow-up data, 7) inclusion of polysomnographic data, as well as anamnestic data, and 8) inclusion of treatment outcome data.

None of the reports reviewed met all of these criteria. Accordingly, we gave the greatest weight to 27 studies that were reported in peer-reviewed journals, had the most subjects, and met most of the criteria (such as diagnostic reliability procedures and inclusion of comparison groups). The task of reviewing this literature was also helped by a recent book chapter by two of us (D.J.B. and C.F.R.) (4), which included 238 references to the English-language literature on insomnia.

RESULTS

The three *ICSD* disorders most closely related to the *DSM-III-R* concept of primary insomnia will be reviewed first: idiopathic insomnia (also known as "childhood-onset insomnia"), sleep state misperception (also known as "subjective insomnia without objective findings"), and psychophysiological insomnia. After the review of these three intrinsic insomnia disorders, we will review the literature related to three *ICSD* extrinsic disorders: inadequate sleep hygiene, insufficient sleep syndrome, and adjustment sleep disorder. Altitude insomnia and environmental insomnia will be briefly touched on, followed by two of the pediatric insomnias, sleep-onset association disorder and limit-setting sleep disorder.

Intrinsic Insomnia Disorders

Idiopathic insomnia. The *ICSD* notes that idiopathic insomnia (*ASDC* "childhood-onset insomnia") is rarely seen in its pure form. The *ICSD* distinguishes it from psychophysiological insomnia, which is diagnosed if the inherent predisposition toward poor sleep is mild and requires the stress of maladaptive conditioning to manifest itself. Idiopathic insomnia is, rather, conceptualized as a more chronic and stable form of insomnia appearing first in early childhood and persisting unrelentingly. The *ICSD* indicates that patients with idiopathic insomnia are psychologically healthy.

The *ICSD* concludes that idiopathic insomnia is a lifelong, serious disorder that cannot be explained by psychological trauma in early childhood or by medical disorders. However, the *ICSD* notes that idiopathic insomnia is likely to be complicated by poor sleep hygiene, learned maladaptive associations, or psychiatric disturbances. This statement raises the possibility of an age-related or developmental continuum in the *ICSD* types of insomnia, as well as the probability of overlap between these proposed types of insomnia.

The best data source for idiopathic insomnia was the 1980 study by Hauri and Olmstead (5), which contrasted 20 patients with childhood-onset insomnia and 39 patients with adult-onset (psychophysiological) insomnia. External validation of the distinction between idiopathic and adult psychophysiological insomnia was provided by polysomnographic evidence of less sleep continuity and less REM density in the childhood-onset group. The authors also reported a higher prevalence of soft neurological signs in the patients with childhood-onset insomnia. A subsequent cluster analysis reported by Hauri (2) supported the distinction between childhood-onset insomnia and persistent psychophysiological insomnia. It is not clear to what extent there may have been overlap of the subjects in the two studies. We could find no replication studies of polysomnographic differences between idiopathic and psychophysiological insomnia, nor could we find studies of controlled treatment trials showing differential treatment response, long-term follow-up studies, data on diagnostic reliability, or family history studies of these two disorders.

Psychophysiological insomnia. The *ICSD* considers psychophysiological insomnia to be an objectively verifiable insomnia due to learned sleep-preventing associations. The patient's focus on the inability to sleep is the hallmark of psychophysiological insomnia. Apparently, compared to patients with idiopathic insomnia or sleep state misperception, patients with psychophysiological insomnia are more likely to have abnormal psychological profiles, involving malaise, guardedness, sensation avoidance, and denial (6–8).

The *ICSD* notes that psychophysiological insomnia lies on a continuum with a number of other diagnostic categories: 1) inadequate sleep hygiene (patients with psychophysiological insomnia still sleep poorly even when they maintain adequate sleep hygiene), 2) dysthymia, 3) generalized anxiety disorder, and 4) idiopathic insomnia. The *ICSD* notes that patients with psychophysiological insomnia have marginal sleep during childhood and adolescence but that they get by. In contrast, patients with idiopathic insomnia sleep consistently poorly during childhood and beyond. At least two studies of patients with psychophysiological insomnia (9, 10) have shown that their electroencephalographic sleep profile differs from that of depressed patients.

Hauri's study (2) had the largest number of subjects, and he reported the results of a cluster analysis of insomnia involving 90 patients. Cluster 1 included both subjects with good sleep and patients diagnosed as having *ASDC* subjective insomnia without objective findings (*ICSD* "sleep state misperception"). Cluster 3 included many older patients with psychophysiological insomnia, while younger patients diagnosed as having psychophysiological insomnia tended to be grouped in other clusters. Clusters 7 and 8 denoted, respectively, moderate and severe childhood-onset insomnia. Clusters 3, 7, and 8 suggest the probability of an age-related continuum in insomnia, rather than necessarily distinct disorders. The existence of idiopathic insomnia (childhood-onset insomnia) has yet to be confirmed prospectively in child patients. All of Hauri's patients, for instance, were diagnosed retrospectively on the basis of their histories of childhood onset. This is not the same thing as identifying the disorder prospectively during the first decade of life.

The importance of Hauri's study lies in the fact that it provides mathematical evidence for the validity of psychophysiological insomnia and childhood-onset insomnia as separate disorders. The question then becomes, Are these distinctions important clinically? If so, how and why? At this time the question is unanswered.

Sleep state misperception. The *ICSD* uses the term "sleep state misperception" to mean a marked discrepancy between the subjective complaint of insomnia and the objective polysomnographic findings. The course and prevalence of sleep state misperception are unknown, but, according to the *ICSD*, it appears to apply to fewer than 5% of all patients with primary complaints of insomnia. In the studies to date, no typical psychological or cognitive disorder has been delineated.

There are probably fewer than 30 well-documented cases of sleep state misperception in the research literature. In a 1985 study of eight patients with sleep state misperception who were contrasted with eight patients diagnosed as having psychophysiological insomnia, Sugerman et al. (11) reported no nocturnal polysomnographic abnormalities in sleep state misperception, but, surprisingly, there was evidence of impaired waking performance on an auditory vigilance task and a tendency for greater daytime sleepiness (as measured with the multiple sleep latency test, a series of five nap recordings at 2-hour intervals from 10:00 a.m. to 6:00

p.m. designed to measure rapidity of sleep onset). The authors noted an absence of detectable psychopathology according to the MMPI. The study did not appear to control for the potentially confounding issue of motivation in the auditory vigilance task, nor did it use structured psychiatric interviewing to rule out the presence of psychopathology in the patients with sleep state misperception. We could find no other reports of treatment data for sleep state misperception, no longitudinal follow-up data, and no data on etiology. Most treatment studies of chronic insomnia probably include some of these patients, as well as patients with psychophysiological insomnia.

We believe that the salient question is, Could sleep state misperception be an extreme example of the tendency of patients with chronic insomnia to underestimate sleep time and overestimate the amount of time it takes them to get to sleep, in comparison with objective laboratory measures? In a study of this issue by Carskadon et al. (12), it was observed that for fewer than one patient in five with a complaint of very short sleep or very long sleep latency was the complaint confirmed in a laboratory sleep setting. The authors speculated that what determines the complaint of insomnia may be how the sleep loss occurs, noting that patients with insomnia have strikingly more arousals, i.e., chronic interruptions of sleep, than normal subjects. Carskadon et al. (12) also noted abnormal MMPI profiles in 58% of their subjects.

Further evidence of the ubiquity of sleep state misperception in chronic insomnia was provided by Frankel et al. (13), who studied 18 patients with chronic primary insomnia and 18 age- and sex-matched comparison subjects. As a group, the patients with insomnia significantly overestimated sleep latency and underestimated time spent asleep and sleep efficiency. It is interesting that the comparison subjects' estimates of these variables tended to be in the opposite direction. As in the study by Carskadon et al., the patients with insomnia in Frankel et al.'s study consistently overestimated sleeplessness. To be sure, polysomnographic findings were significantly correlated with subjective estimates, but the polysomnographic findings did not necessarily explain the severity of the patient's complaint. The authors felt that night-to-night variability is critical and that the unpredictability of sleep is more important than sleeplessness-related anxiety in the pathogenesis of insomnia.

In Hauri's cluster analysis (2), patients with good sleep and patients with subjective complaints of insomnia without objective findings were assigned to the same cluster. When both clinical and laboratory predictor variables were used, the two groups of subjects were not separated.

It seems reasonable to suggest that we do not know what factors determine subjective estimates of sleep quality or quantity. Perhaps the most conservative interpretation of the existing data is that sleep state misperception is a prevalent characteristic of chronic insomnia generally, and, hence, patients diagnosed with sleep state misperception may simply lie at one end of a continuum.

Does the diagnosis of sleep state misperception (subjective insomnia without objective findings) have implications for long-term course or treatment? At this time the question is unanswered.

Extrinsic Insomnia Disorders

Inadequate sleep hygiene. In the *ICSD*, disorder of sleep hygiene is constituted by various habits and activities of daily living that may promote a sleep difficulty—for example, ingestion of caffeine or taking naps at different times of the day. The *ICSD* recommends that sleep hygiene be evaluated in the context of every insomnia to determine how much of a contribution it is making in sustaining the sleep disturbance. The *ICSD* also notes that sleep hygiene "violations" may not reach sufficient severity to produce insomnia. Rather, in most cases a confluence of factors, including inadequate sleep hygiene, produces a clinically significant insomnia. The *ICSD* states that the usual polysomnographic features associated with sleep continuity disturbance also characterize patients with inadequate sleep hygiene. In other words, there is nothing distinctive about the polysomnographic findings in patients for whom inadequate sleep hygiene is apparently the major etiologic factor.

The *ICSD* cites a 1987 study by Spielman et al. (14) of sleep restriction therapy as supporting the existence of a disorder of inadequate sleep hygiene. In fact, however, the Spielman et al. study appears to be predicated on the belief that excessive time in bed is "one of the important factors that perpetuates insomnia" rather than being a primary cause. Moreover, the 12 subjects with persistent psychophysiological insomnia showed the same pattern of change as the entire group, including 21 patients with psychiatric insomnia. The authors concluded, "The similarities in outcome were more prominent than any differences between the diagnostic groups." Hence, no differential response to treatment was noted as a function of presumed diagnostic subtype. In a study of 44 patients with sleep-onset insomnia, 49 patients with sleep-maintenance insomnia, and 50 subjects with good sleep, Lacks and Rotert (15) found that although the patients with insomnia had better knowledge of sleep hygiene than the comparison subjects, both insomnia groups had more deficient sleep hygiene practices regarding nicotine, sleep medication, alcohol, and exercise. The authors also noted, "Hygiene practice needed most improvement in the areas of regular exercise, pre-bedtime relaxation, and managing bedtime worry." The results suggested that poor sleep hygiene is not a primary cause of insomnia but may play a role in exacerbation.

We could find no empirical evidence for the existence of an independent disorder of inadequate sleep hygiene. Rather, inadequate sleep hygiene appears to be a complication of other types of insomnia and appears mainly to be an important contributing factor in the perpetuation of insomnia. On the basis of studies by Spielman et al. (14) and by Lacks and Rotert (15), one must also ask whether inadequate sleep hygiene does not overlap considerably with other forms of insomnia, such as insomnia related to drug abuse or psychophysiological insomnia.

Insufficient sleep syndrome. In the *ICSD*, the concept of insufficient sleep syndrome appears to be grounded primarily in experimental work investigating the effects of sleep deprivation and sleep restriction on physiological sleepiness the next day and on measures of mood and performance. Probably the best investigations in this area have been done by Carskadon and Dement (16) and Friedmann et al. (17). It should be noted that the initial complaint associated with insufficient sleep is more often daytime sleepiness than insomnia.

The major question is whether it is clinically useful and valid to conceptualize insufficient sleep—like poor sleep hygiene—as a separate disorder, or whether it makes more sense to consider insufficient sleep to be an important contributor to complaints of insomnia and excessive daytime sleepiness (18). If it were shown that some individuals have 1) short sleep duration despite adequate opportunity to sleep, 2) otherwise normal sleep study results, and 3) an objectively verified complaint of excessive daytime sleepiness, then a disorder of insufficient sleep would be more strongly supported. However, our literature review does not show this, and we must conclude that insufficient sleep syndrome should be conceptualized as a behavioral pattern leading to a complaint of insomnia or excessive sleepiness, rather than a nosologically distinct disorder separate from other types of insomnia.

Adjustment sleep disorder. The *ICSD* uses the term "adjustment sleep disorder" to denote transient or short-term insomnia that is a reaction to stress (see reference 19). Hence, the symptoms should remit if the stressor is removed and/or the level of adaptation is increased. The central distinction between psychophysiological insomnia and adjustment sleep disorder is the presence of an identifiable stressor in the adjustment disorder.

In our opinion, the best controlled study relating to adjustment sleep disorder is probably that of Cartwright (20), even though this study is not cited in the *ICSD* bibliography. Cartwright's study focused on dream reports and REM sleep changes during and after a mood-disturbing event, i.e., divorce. This study suggested that sleep physiology alterations attending a mood-disturbing event might be long-standing, particularly in patients who react with depression. Cartwright's finding of protracted sleep disturbance after divorce was similar to self-report data in longitudinal studies of bereavement, such as that of Clayton et al. (21), who reported sleep disturbance to be a persistent (>1 year) and disabling symptom in 48% of subjects whose spouses had died. Finally, in a questionnaire study involving 243 respondents, Hartmann and Brewer (22) found that one major factor associated with an increased need for sleep was "mental or emotional stress," which correlated strongly with changes of occupation, increased mental activity, and depressed mood.

Does it make sense to distinguish the *ICSD* diagnosis of adjustment sleep disorder from the *DSM-III-R* categories of adjustment disorder with or without depressed mood and bereavement with or without complications? Would such a distinction be useful to clinical psychiatrists? If so, how? It may be possible to have a stress (e.g., medical procedure, life event) that does not lead to mood or behavioral sequelae but has insomnia as the core symptom. It is the nature of the stressor (and its meaning to the patient) that will have implications for the duration, severity, and management of the sleep complaint.

Altitude insomnia and environmental insomnia. Altitude insomnia in small groups of volunteers has been well described clinically and polysomnographically (see references 23 and 24). It usually develops at elevations greater than 4,000 meters and may be related to normal physiological control of respiration in the presence of low inspired oxygen. The interpretation of the data appears to be partly confounded by environmental factors, such as cold, altered light/dark cycles, and possibly jet lag. In the *ICSD*, the concept of environmental sleep disorders is based on a handful of studies investigating the impact of ambient noise (see reference 25) and extreme temperature change (see reference 26) on sleep.

While these studies are of considerable experimental and scientific interest, their clinical relevance to psychiatry appears to be limited.

Sleep-onset association disorder and limit-setting sleep disorder. The *ICSD* conceptualizes both of these sleep disorders as pertaining mainly to childhood (27, 28). Both represent useful clinical constructs, popularized by Ferber (29), who wrote a self-help book for parents related to these disorders but who has not, according to our literature review, published any empirical studies. Both disorders may be conceptually similar to psychophysiological insomnia insofar as both may be related to conditioning factors adverse to sleep. In this sense, the distinction from adult psychophysiological insomnia is not supported by published empirical data. Again, it appears parsimonious to suggest that we may be dealing with an age-dependent continuum of insomnia, in which a common etiologic denominator may be adverse conditioning factors.

DISCUSSION AND RECOMMENDATIONS

The *ICSD* subtypes of chronic intrinsic ("primary") insomnia are clinically appealing and represent the accumulated wisdom, the consensus, and the working diagnoses of clinical investigators and sleep disorder specialists. In our view, the *ICSD* subtypes embody the clinical belief that complaints of insomnia are multifactorial and that consequently treatment approaches need to be individually tailored to the specific constellation of factors found in a particular patient (30, 31). The concepts of etiologic heterogeneity and need for treatment specificity are further supported by the work of Jacobs et al. (32), who reported that polysomnographic findings resulted in the modification of the clinical diagnosis of chronic insomnia in approximately 50% of 123 consecutive patients with chronic insomnia. The concepts of heterogeneity in etiology and treatment specificity were also articulated by the 1984 National Institute of Mental Health consensus conference on drugs and insomnia (33).

Despite the clinical utility of the *ICSD* distinctions and despite the probable heuristic value, the available empirical data on the reliability and validity of these subtypes are limited and therefore do not yet provide a compelling basis for abandoning the *DSM-III-R* concept of primary insomnia. The clusters reported in Hauri's 1983 study (2) need to be replicated, and their clinical validity needs to be demonstrated in studies of etiology, family history, response to treatment, and/or long-term course. It would serve a useful educational purpose to discuss the subtypes (idiopathic insomnia, sleep state misperception, and psychophysiological insomnia) in the *DSM-IV* text relating to primary insomnia and to discuss the putative roles of sleep hygiene, insufficient sleep, and environmental factors in case formulation. Similarly, the clinical importance of duration of complaint should be underscored in the text because of the greater probability of finding stressors in the lives of patients with recent-onset insomnia. The nature of the stressor, such as bereavement, will have important implications for the severity, duration, and complications of the sleep complaint and for its management. In a similar spirit of clinical relevance, pediatric sleep disturbances related to parental behaviors could be usefully discussed in the *DSM-IV* text. The information concerning the apparent effects of altitude change on sleep and breathing might be mentioned in the text here or discussed in relation to insomnia and medical disorders, where it seems more relevant.

In conclusion, we recommend retaining the *DSM-III-R* concept of primary insomnia and not adopting the *ICSD* subtyping of insomnia at this time. The *ICSD* subtyping usefully addresses factors that may be important in insomnia. As such, these factors should be considered in the text. However, on the basis of the existing empirical studies, if we were to elevate factors that disturb sleep to disorders, we might be reaching premature conclusions. At the same time, although the use of a single diagnostic category precludes the premature adoption of more differentiated diagnostic categories, it may lull clinicians into a false sense of security that might lead them to overlook clinically important heterogeneity. Accordingly, one might use the term "primary insomnias" rather than "primary insomnia" and start with two primary insomnia categories, namely, idiopathic insomnia and psychophysiological insomnia. Although our literature review does indicate there may be valid distinctions between them, we have also suggested that further empirical validation is necessary. Such studies are crucial, we believe, to achieving the long-term goal of identifying the various clinical entities which constitute this category. The *DSM-IV* text should provide description of some of these entities and commentary on their potential strengths and weaknesses.

One further recommendation is in order. We do not know of any published data on the performance characteristics or the clinical and research utility of the *DSM-III-R* classification of insomnia. In a pilot field trial at the University of Pittsburgh involving a review of 19 cases of chronic insomnia by six raters, interrater reliability appeared to be higher in the application of the *DSM-III-R* criteria than for the *ASDC* (1979) criteria (unpublished data). This is perhaps not unexpected, since *DSM-III-R* "lumps" and *ASDC* "splits." On the other hand, it is also our impression that the treatment recommendations based on *ASDC* diagnoses were perhaps somewhat more targeted, or focused, than the treatment recommendations based on *DSM-III-R* diagnoses. Hence, we support field trials to evaluate the relative performance characteristics and the utility of the *DSM-III-R* "lumping" approach versus the *ICSD* "splitting" approach. Furthermore, assessment of the level of clinician expertise (sleep disorder specialist versus general psychiatrist) on interrater agreement in the application of the *DSM-III-R* and *ICSD* systems is recommended. Finally, the effect of knowledge of polysomnographic data on rates of agreement in the application of the *DSM-III-R* and *ICSD* systems needs to be assessed. It is conceivable that these data would lead to the incorporation of some *ICSD* subtypes (e.g., psychophysiological versus idiopathic) into *DSM-IV* and, at the least, would inform the discussion of these subtypes in the text.

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Biological Correlates of Mental Activity Studied With PET

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The development of newer imaging techniques that allow direct investigation of the function of the human brain under normal and pathological conditions has affected the way in which we conceive of the mind/brain relation. In this report the authors use examples from findings obtained with positron emission tomography (PET) to illustrate the highly interactive organization of the brain. Because operations in the brain require the participation of various brain areas, a model that does not require a one-to-one relationship between the physical and mental, but rather allows an association between clusters of physical processes and one or more mental phenomena, may reflect better the relation between physical brain phenomena and mental activities.

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As new techniques for investigating the human brain develop and new knowledge emerges, we are faced with the need for models of the brain that can incorporate these findings. Previous models that separated "mental" from "physical" phenomena have been inadequate in exploring the relation between these two processes (1). The failure can be attributed to both biological and philosophical reasons. The biological reasons have to do with the way neuroscientific knowledge has been obtained. That is, most of the studies were conducted 1) with animals, which lack the complexity of human behavior, 2) with patients suffering from brain disorders, in whom by definition brain function is disturbed, or 3) with pieces of brain tissue, in which the nature of the phenomenon is isolated from the rest of the brain.

The philosophical reasons relate to the inadequacy of a model that attempts to construct a direct relation between specific biological and mental states without consideration of the multiplicity of biological phenomena that have to occur simultaneously to generate a specific behavior or mental activity (2). In this respect, a model that does not require a one-to-one relationship between the physical and mental, but instead allows for a cluster of physical activities which relate to one or more mental phenomena (associations by ipsicorrespondence), may reflect better the relationship between physical and mental activities.

The recent development of functional imaging technologies, such as positron emission tomography (PET), single photon emission computed tomography (SPECT), computerized electroencephalography, and magnetoencephalography, allows direct evaluation of the function of the brain in normal living human beings and its disruption in the mentally ill. These imaging technologies have started to breach the biological limitations imposed by the inaccessibility of the human brain (3).

In this paper we will use the findings obtained with PET to illustrate how 1) operations in the brain are processed serially and/or in parallel, involve simultaneous and sequential participation of various brain structures, and are organized into highly specific functions and how 2) functional brain imaging techniques, such as PET, will help us understand the operations of and correlations between the mind and the brain.

In approaching this material we will first describe PET technology, then we will examine, using PET examples, certain features of the brain involving its organization and its disruption by disease that help us understand how the brain processes information serially and/or in parallel, and, finally, we will relate these findings to the brain/mind interaction.

POSITRON EMISSION TOMOGRAPHY

PET measures the concentration of positron-labeled compounds within the brain. Since positron emitters can be used to label compounds that are physiologically active, these agents can be used to directly measure brain function and neurochemistry. The most frequent variables measured with PET have been glucose metabolism and cerebral blood flow (CBF). Sokoloff's work with autoradiography and deoxyglucose, an analogue of glucose, laid the foundation for use of deox-

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yglucose to measure brain glucose metabolism with PET (4–6). CBF can be measured with PET by means of different strategies (7, 8). Measurements of glucose metabolism and CBF are used to monitor brain function because of the physiological coupling of CBF, glucose metabolism, and neuronal activity (5, 9). The examples reported in this paper are from studies measuring regional brain glucose metabolism or CBF. The methodological limitations of these studies are due to the limited spatial resolution (6.0 mm in plane, 6.5 mm in axial) and temporal resolution (40 seconds for CBF and 30 minutes for glucose metabolism) of PET (10). This means that PET can only evaluate activation of relatively large areas of the brain and that it can only obtain information about activation over a relatively long period, which does not distinguish serial from parallel brain regional activation. On the other hand, PET allows investigation of the human brain in vivo and repeated measurements on the same subject.

The use of PET to measure receptor concentration, enzyme concentration, and neurotransmitter synthesis and its applications in the investigation of the human brain will not be covered in this paper. A detailed description of the PET procedure and the different positron-labeled radiopharmaceuticals used to measure receptors, enzymes, and substrate metabolism is out of the scope of this paper and can be obtained from reviews of these topics (9–11).

BRAIN ORGANIZATION

Brain organization refers to the association among the various brain areas as they interact with each other to receive, process, and integrate the internal and external experiences of the individual.

Three principles basic to understanding brain organization have been identified. The first is the highly interconnected pattern of brain organization (12). This property permits the brain to process a given stimulus simultaneously in different brain areas and to provide an integrated analysis of the stimulus (13). It also incorporates the notion that any given task performed by the brain involves a large number of brain areas, each of which performs a specific operation. This means that even a simple behavior is the result of a multitude of brain areas functioning coordinately with one another (14, 15).

The second principle is the hierarchical structure of this organization, which allows filtering of irrelevant information and channeling of various stimuli into the appropriate brain areas (16). For certain brain areas, such as association cortex and prefrontal cortex, this organization appears to be not hierarchical but highly interactive, and feedback pathways affect the processing of information at different levels of the system (17).

The third principle relates to the concept of functional differentiation. This means that particular brain areas are responsible for specific functions (15). Because of the highly interconnected pattern of brain organization this concept should be kept in mind when designating a particular area as responsible for a given function, since this area may be just a part of a more complex system.

The highly interconnected pattern of brain organization can be investigated with PET and has been studied for the visual system. These studies have started to map the brain areas other than occipital cortex that participate in the processing of visual information. One study which evaluated brain activation by patterned visual stimulation revealed that visual stimulation not only activated the occipital areas but affected several other brain areas (18). As expected, unilateral visual stimulation increased metabolism of the contralateral striatal cortex. It also increased metabolism of the right inferior parietal and right superior temporal cortex independent of the side of visual stimulation. Activation of these right cortical areas suggests the participation of these areas in a functional system for processing visual stimuli (19). Involvement of subcortical structures in the processing of audiovisual stimulation has also been demonstrated with PET (20).

The hierarchical structure of the brain can be investigated with PET. By using a given stimulus and varying its complexity, one can map out the hierarchical order of the various brain areas that process the stimulus. This was first demonstrated in a PET study that tested subjects with three visual stimuli of increasing complexity: a bright light, a black and white checkerboard pattern, and an outdoor visual scene. An increase in the complexity of the visual stimulus was associated with a concomitant increase in the activation of the primary and associative visual cortex (21).

The principle of functional differentiation can be investigated with PET by stimulating the subject with stimuli composed of very specific features to map the different constituents of a given functional system. An example of such a strategy is a PET study that evaluated cortical activation during various behavioral language tasks. This study demonstrated involvement of separate brain areas for the processing of words presented visually and auditorially and involvement of the same brain areas for the processing of semantic and articulation codes (22). Visual presentation of words activated striatal cortex and prestriatal areas. Although activation of striatal cortex occurs with several visual stimuli, the activation of the prestriate has so far been demonstrated only by visual presentation of words. Auditory presentation of the words activated primary auditory cortex, left temporoparietal cortex, and left anterior superior temporal cortex. When the subjects were asked to repeat the words presented irrespective of mode of presentation, there was additional activation of areas involved in semantic processing—the left inferior frontal cortex and anterior cingulate gyrus (22). In this way PET studies are starting to map the brain areas that constitute the systems involved in processing different types of stimuli (23, 24).

Differences among individuals in the strategies used to process a given stimulus need to be taken into consideration when relating the activation of a set of brain areas to a given stimulus. This was illustrated in a PET study that showed differential activation of left versus right cortical areas in subjects asked to perform a tonal memory test (25). Individuals who recalled the tone by using an analytical strategy activated the left hemisphere, whereas subjects who used a nonanalytical approach to perform the task activated the right hemisphere. This study demonstrates different patterns of activation in response to the same stimulus due to the differences in the individual strategies employed to perform the task.

EFFECTS OF BRAIN DISEASES ON BRAIN ORGANIZATION

Evaluation of the effects of a well-localized brain defect on brain function can provide valuable insight about the interactions of a given region. PET studies of patients suffering from localized brain pathology have been able to show how dysfunction of a given brain area can have repercussions for other brain areas. This phenomenon, referred to as "diaschisis," appears to be the result of disruption in the interaction among brain areas secondary to a disruption in one of the areas of the communication pathway. In a study of aphasic patients with left vascular hemispheric lesions (26), close to 50% of the patients showed not only hypometabolism in the damaged hemisphere area but also in the contralateral cerebellum. Similar disruptions in the corticocerebellar pathway have been demonstrated in patients with a wide variety of lesions (27–30). Disruptions in thalamocortical, interhemispheric, and intrahemispheric connections have also been documented with PET in patients with localized vascular pathology (31, 32).

Activation studies of patients with well-localized defects is another strategy used to evaluate brain organization. An example of such a strategy is a study of patients with amblyopia (33). Amblyopia is a defect in visual acuity caused by visual deprivation or visual dysfunction in one of the eyes during a crucial period of development (34). Animal models of amblyopia have demonstrated a reduction in the visual cortical neurons that respond to the amblyopic eye (35). Although the structural changes in the brains of amblyopic patients have not been confirmed, there is good reason to believe that they are similar to what is seen in animal models of amblyopia. The disease provides an opportunity to study the effects of unilateral dysfunction of the visual system on the general pattern of brain organization. As expected, when studied with unilateral visual stimulation, patients with amblyopia showed less activation of the primary visual cortex when the amblyopic eye was stimulated. However, the accessory visual cortex was activated irrespective of stimulation of the sound or the amblyopic eye (33). In addition, unilateral visual stimulation with a complex visual scene induced activation of the contralateral frontal and temporal cortex, which also occurred irrespective of whether the sound eye or the amblyopic eye was stimulated and was similar for normal subjects and amblyopic patients. These results suggest that activation of brain areas which process these visual stimuli can occur even with failure to activate the primary visual cortex and that most of these processes occur in parallel, since the amblyopic patients showed activation of these areas even when the amblyopic eye was stimulated.

The capacity of the brain to respond to stimulation relies in part on its hierarchical organization, which allows it to filter information and to relay that information to the appropriate brain regions. Disruption of the filtering and relaying processes can lead to defects in the ability to interact with the environment (36). As a result, either the external environment takes precedence over the individual's own desires and triggers behaviors that are the result of previously automated routines in the brain or the internal environment elicits behaviors that are discordant with the external environment. This type of pathology is seen in obsessive-compulsive disorder (37), where the reaction to the internal or external environment takes precedence over the conscious needs and desires of the individual. Before the development of functional imaging techniques it was not feasible to disclose the brain derangements associated with obsessive-compulsive disorder. Preliminary PET studies are starting to map the areas of the brain that are dysfunctional in patients with obsessive-compulsive disorder. These studies have documented abnormal function of orbital frontal cortex and caudate in obsessive-compulsive disorder patients (37, 38). These findings are in agreement with those from studies of ablation in animals, which document repetitive compulsive behavior after destruction of the caudate nuclei or the orbitofrontal cortex (39). It has been postulated that a circuit which involves orbitofrontal cortex, caudate, ventral pallidum, and medial thalamic nucleus serves a critical role in the pathogenesis of obsessive-compulsive disorder (40). In addition, this circuit interacts and has multiple connections with limbic structures (40), so derangements in areas of the brain related to behaviors needed for self-preservation or species survival, such as grooming and territoriality (41), could, if disrupted, generate the emergence of these behaviors automatically and independent of any exterior stimulation (36).

BRAIN/MIND RELATION

These PET studies have shown that operations of the brain are associated with activation of various brain areas and that a functional specificity for these operations exists. In trying to correlate these findings to understand the relation between the mental and physical, it becomes evident that trying to associate any particular brain area with a given mental operation is not feasible because mental operations are the result of coordinated activation of various brain areas. Furthermore, a given brain area probably participates in more than one mental operation, as is illustrated by the activation of the left inferior frontal cortex and anterior cingulate gyrus by both the visual and auditory presentation of words. The organization of the brain into highly coordinated functional systems explains why defects of different brain areas can generate the same type of mental dysfunction. This is exemplified by the case of obsessive-compulsive disorder, in which, because of the multiple connections of the orbitofrontal cortex with basal ganglia, thalamic nuclei, and limbic structures, lesions in different areas of this circuit could generate perseverative behaviors.

Another possibility that needs to be taken into consideration when relating a given regional defect to dysfunction of a particular mental operation is that the mental dysfunction could relate not only to the defect per se, but to the disruption of a brain area which is connected to the area where the primary defect is located. This is shown by the PET studies documenting hypometabolism in brain areas far from the original lesion.

In interpreting these findings, one should also keep in mind the reductionism of this approach and consider that multiple mental operations are occurring at the same time at a given moment for a particular individual. Activation of a particular brain area may be the result of the task investigated, but it may also represent activation due to its interactions with other functional systems. Similarly, differences among individuals in strategies used to process a given stimulus may lead to differences in the patterns of activation in response to the stimulus.

Finally, PET is limited by its temporal resolution and produces no information with respect to temporal sequencing of brain processes. Techniques such as EEG and magnetoencephalography are better for differentiating between serial and parallel activation of cerebral structures.

SUMMARY

Using PET to investigate brain function has started to reveal various physical processes that seem to correspond in a more direct way with processes in the mental realm. This relation cannot be described as a direct one-to-one correspondence; rather, a cluster of physical processes can be correlated with a group of mental operations. The PET examples we have described have demonstrated the association between particular patterns of brain activation and specific mental processes. However, more work needs to be done before causal links can be established. Also, the examples described have focused mainly on simple mental operations; in the future, with further improvements in imaging technologies it may be feasible to investigate more complex mental phenomena. Although the PET studies are limited by the spatial and temporal resolution of the instrument, the feasibility of directly investigating regional brain activation by mental tasks in humans and of evaluating the effects of localized brain defects on the cerebral activation elicited by specific tasks opens up the opportunity to create models that take into account the functional organization of the brain. These developments may lead to a better understanding of complex and higher-order human processes.

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Monitored Conditional Release of Persons Found Not Guilty by Reason of Insanity

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This article reviews the recent literature documenting changes that have taken place in the management and treatment of insanity defense acquittees with the development of conditional release and monitored community treatment. The review demonstrates that conditional release is particularly important as a means of balancing the protection of society with the treatment of insanity defense acquittees in the least restrictive environment. The review also highlights the development of community programs based on treatment models for the chronically mentally ill. In addition, monitored community treatment programs appear cost-effective when compared with hospital-based programs. These factors point to the development in the 1990s of program standards for the release of insanity defense acquittees.

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This paper explores 1) the question of the release of persons found not guilty by reason of insanity from hospitals into the community and 2) how this can be achieved on a practical basis while balancing the public policy interests of societal protection and individual rights. The dilemma posed by the release of insanity defense acquittees was clearly illustrated by *State v. Fields* in New Jersey:

> If at any periodic review proceeding the State is unable to meet its burden of justifying the continuance of the currently prevailing restraints upon the liberty of the patient, it becomes the task of the reviewing judge again to "mold" an appropriate order. . . . The new order should provide for the least restrictive restraints which are found by the judge to be consistent with the well-being of the community and the individual. . . . However, even where the [patient's] condition shows marked improvement, only the most extraordinary case would justify modification in any manner other than by a gradual de-escalation of the restraints upon the [patient's] liberty. (1)

Although it is generally accepted that this balance between protection and liberty must be struck, there is great difficulty in implementing workable release procedures that can achieve these goals. In our view, conditional release, which allows insanity defense acquittees to be released from hospitals into monitored community treatment programs, is the most acceptable mechanism for meeting the policy goals described in *State v. Fields*.

Tensions between protection of the public and least restrictive treatment of the patient are built into all the major law and mental health interactions, from voluntary hospitalization and civil commitment on one end of the continuum to the criminal justice system on the other. Along this continuum, different weights are given to factors related to protection and treatment in least restrictive settings. In voluntary hospitalization, the primary focus is on treatment. In civil commitment, treatment is also the most important focus, although this has been greatly attenuated in the past 20 years with the increasing focus on dangerousness as the major criterion both for hospitalization and release (2, 3). This increased focus on protection of the public has been further emphasized in the legal doctrine of the

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duty to protect emanating from the *Tarasoff* decision (4, 5). In the criminal justice system, protection is even more heavily weighted, and there is less emphasis on treatment concerns (6).

RELEASE PROCEDURES AFTER THE INSANITY DEFENSE

Procedures governing the release of insanity defense acquittees have tended to occupy the middle ground between traditional civil commitment and criminal justice system models. However, over the last three decades, this ground has not been constant, as release procedures first moved closer to the civil commitment model and then, in more recent years, moved toward the criminal justice system model. The major changes in civil commitment statutes in the late 1960s and early 1970s, with their increased focus on individual rights and current dangerousness (7–9), drew insanity defense procedures along with them. In some jurisdictions this resulted in the application of civil commitment standards to the release of insanity defense acquittees.

Prior to the pivotal case of John Hinckley, Jr., in 1982, dissatisfaction with various aspects of the insanity defense was already being expressed (10). This dissatisfaction was exemplified by the adoption of the "guilty but mentally ill" verdict, first implemented in Michigan (11), the alteration of the insanity defense in Montana (12), and the introduction of the Psychiatric Security Review Board in Oregon in 1978 (13).

The *Hinckley* case (14) dramatically shifted the weight given to protection of the public and drew the management of insanity defense acquittees even closer to the criminal justice model. Three major professional organizations rapidly published position papers calling for restrictions on the insanity defense (15–17 and American Medical Association resolutions 15 and 21, 1983). These reactions to *Hinckley* led to important changes in federal statutes (18) and statutory changes in many jurisdictions (19, 20). Eight states subsequently adopted the more restrictive option of guilty but mentally ill, bringing the total number of such states to 12 at the end of 1985 (20). In several jurisdictions, a number of other changes occurred in the dispositional provisions for insanity defense acquittees, including the provisions governing length of commitment and release through court proceedings or more traditional civil commitment proceedings (21).

Another important influence on release procedures came from the 1983 U.S. Supreme Court decision in *Jones v. U.S.* (22), which upheld the right of states to commit a person acquitted by reason of insanity for an indefinite period, as long as the individual remains mentally ill and dangerous.

Now, in the 1990s, public policy has shifted toward protection. However, the legitimate civil liberty interests of insanity defense acquittees need to be recognized and a balance achieved. A system that places too much emphasis on protection of the public runs the risk of unfairly confining an individual beyond the period when confinement is necessary for treatment, a form of "preventive detention" (23) in psychiatric facilities. In addition to the important question of individual rights, inordinately long and potentially unnecessary hospitalization results in substantially higher costs at a time when mental health funds are desperately needed in the public sector (24). On the other hand, insufficient weight given to protection may result in an unrealistic view of the typical insanity defense acquittee's ability to live independently in the community (25–29) and an underestimation of the danger that the mentally ill may present to society (30).

Between the extremes it seems that concerns about public protection, individual rights, and cost are best handled in a system that is designed to give serious consideration to both protection and liberty. Such an approach would provide the largest gain in public protection together with the largest gain in individual liberty, and at the same time it would provide a significant gain in mental health treatment.

OREGON'S PSYCHIATRIC SECURITY REVIEW BOARD

The following description of the Oregon Psychiatric Security Review Board is presented as an example of a comprehensive program for the management and treatment of persons judged not guilty by reason of insanity. Conceptually similar programs are developing in other jurisdictions.

In the mid-1970s, Oregon reexamined its procedures governing the release of insanity defense acquittees. There was growing public and professional concern that the system placed the public in jeopardy because of premature hospital release and lack of community monitoring of conditionally released patients. After several years of study, the 1977 legislature created the Psychiatric Security Review Board (31) as a means of addressing the concerns regarding the release of insanity defense acquittees.

The board is composed of five part-time members and functions independently of the court system. Once a person is assigned to its jurisdiction, the board assumes sole authority to determine client placement, either in the hospital or on conditional release in the community. The trial court judge determines the maximum length of jurisdiction of the board on the basis of the sentence that the individual might have received had there been a finding of criminal responsibility. We have referred to this as the "insanity sentence" (32). The trial court judge also determines whether the initial placement will be in the forensic hospital or in the community on conditional release.

The board controls placement and movement between hospital and community through procedures that govern conditional release and revocation of conditional release. The board may discharge an individual before the end of its jurisdiction, but it is required to discharge an individual once the period of jurisdiction elapses.

The Oregon Psychiatric Security Review Board has been especially important in developing the large-scale and systematic use of conditional release and monitored community treatment. The board closely coordinates its activities with the Oregon Mental Health and Developmental Disability Services Division. The division is responsible for providing psychiatric treatment for insanity defense acquittees either in the forensic hospital or on conditional release in the community. Community services are secured by means of contracts between the division and community mental health service providers. Funds are contracted to specific programs for the care of specific individuals—a type of capitated funding system (24).

While developing the conditional release program, the Oregon board nonetheless retains an overall orientation toward protection of the public, and thus it is representative of the direction taken in many jurisdictions. Oregon statutes state, "In determining whether a person should be committed to a state hospital, conditionally released or discharged, the Board shall have as its primary concern the protection of society" (33). In addition to this statutory mandate, the Oregon Supreme Court upheld this legislative priority in a widely reported case, *Cain v. Rijken* (34).

CONDITIONAL RELEASE

In our opinion, the development of the conditional release of insanity defense acquittees into monitored community treatment programs was a major advance in the 1980s. Conditional release, monitored community treatment, and the availability of workable revocation procedures provide a practical means of addressing the issue of balanced dispositions for insanity defense acquittees. In addition to our work in Oregon (35, 36), there are data from Maryland (37, 38), Illinois (39, 40), California (41, 42), New York (43), Washington, D.C. (44), and a recent review article (45) that support this position.

The availability of conditional release and monitored treatment is extremely important in both a conceptual and a practical way in several critical areas related to the question of hospital release.

1. Prediction of dangerousness. There is no single topic in the interaction between law and mental health issues that has raised more concern than the accuracy of predictions of future dangerousness. The inaccuracy of such predictions was brought forcefully to the attention of behavioral scientists after the *Baxstrom* decision in 1966 (8, 46). The dominant position in the scientific community now is that a long-term prediction cannot be made with any acceptable degree of accuracy (47–49).

An effective mechanism for conditional release and revocation makes the issue of predicting dangerous behavior less pressing. A treatment system that has limited community options will inevitably be pressed into placing greater weight on the prediction of dangerousness because of the substantial negative consequences of an erroneous release. Given the difficulty in predicting dangerousness, such systems will tend to hospitalize more individuals for longer periods of time. Having an option to use conditional release with supervision and prompt revocation if necessary gives the decision maker more latitude in relation to future dangerousness. This system is designed to compensate for the inaccuracy of predictions of dangerousness, thus reducing their importance.

2. Monitored community treatment program. Another major advance in the 1980s was the development of more focused community treatment programs for the chronically mentally ill. These programs are critically important for insanity defense acquittees, since it appears that a large number of them are chronically ill (25, 50–52). Community programs based on the principles of psychosocial rehabilitation are critical to the treatment of patients with chronic mental illness (28, 29, 53).

The treatment approach to the chronically ill patient is applicable to the chronically ill person acquitted by reason of insanity. For example, in the Oregon system, a conditional release plan spells out the agreement among the Psychiatric Security Review Board, the Mental Health and Developmental Disability Services Division, the community program, and the insanity defense acquittee regarding conditional release. The plan contains provisions for housing, case management, and psychiatric treatment. The case manager also sends progress reports to the board on a monthly basis and if an emergency arises. The conditional release plan may also specify special conditions, such as prohibitions against driving, use of alcohol or drugs, and/or contacts with certain persons. Violation of the release plan can lead to immediate revocation of the conditional release order and the return of the individual to the forensic hospital.

3. Costs of hospitalization. Finally, from another public policy viewpoint, conditional release is a potentially cost-effective means of managing these patients, with their high utilization of resources (24). This is a critical concern, since mental health resources are finite, and hospital care is more expensive than care in the community. If the goals of striking a balance between protection of the public and treatment of the individual in the least restrictive environment can be achieved with an additional benefit of cost savings, then the resulting program should have a great deal of appeal to policy makers. We calculated costs of conditional release and monitored community treatment and compared those costs with those of a hypothetical program lacking that option (24). In our model, conditional release substantially lowered costs; community care was estimated to cost about 14% of the costs of the hospital stays it replaced.

DISCUSSION

We have attempted to define the major changes during the past decade in procedures for release of persons acquitted by reason of insanity. The traditional task of balancing protection of society with the civil liberty interests of insanity defense acquittees remains a continuing challenge. In most jurisdictions, the protection of society has assumed dominance over the acquittees' liberty interests. Although protection of society was emphasized during the 1980s, great strides were made during this period in the treatment of these persons.

The Oregon Psychiatric Security Review Board remains an important national model. Originally cited in a 1983 APA position paper (15) as a potential national model, the board still attracts a high level of interest. In 1985 Connecticut became the second state to implement a psychiatric security review board. In 1989 Utah passed analogous legislation, and such legislation is now pending in Kentucky and Florida. Each of these states has found it worthwhile to consider establishing a centralized body to handle matters involving insanity defense acquittees. This centralization of authority allows the development of policy, expertise, and experience that is not possible to achieve when these decisions are left in the hands of a diverse group of trial court judges.

Beginning in Maryland and Oregon, we have seen the systematic development of structured community care for insanity defense acquittees. Conditional release procedures and monitored community treatment, with the availability of prompt revocation procedures, are the hallmarks of this system. Monitored community treatment allows for the protection of society and at the same time serves the liberty of the insanity defense acquittee by developing treatment in the least restrictive setting. These programs are also cost effective when compared to hospitalization, which is an extremely important point in view of the increasing dilemma of funding mental health services.

In addition, the melding of procedures that allow for monitored community care with a developing treatment technology for chronic mental illness is a significant step forward in the treatment of insanity defense acquittees. Community programs designed to reflect the needs of patients with chronic mental illness control some of the situational factors that might lead to violence, and these programs make the prediction of dangerousness less critical in release decisions. Further, lessons learned from monitored care of this population can inform the developing area of outpatient civil commitment.

The conclusions drawn from the growing body of experience in states with monitored treatment will result in the development of standards for programs for the care of insanity defense acquittees. Most state forensic systems still concentrate resources on inpatient services. According to the evidence marshaled for this paper, such systems inadequately address the legitimate civil liberty interests of a large number of insanity defense acquittees who could be safely treated in monitored community treatment programs. Many states will have to work to meet the standards that are currently being developed.

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Effects of Statutes Requiring Psychiatrists to Report Suspected Sexual Abuse of Children

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Objective: Reporting of child sexual abuse is mandatory in all 50 states. Conceptual distinctions between privileged communications and mandatory reporting are reviewed, and the impact of recent changes in Maryland's reporting laws is examined. Method: Beginning in 1964 Maryland law required reporting if abuse was suspected when a physician examined a child. In 1988 reporting of disclosures by adult patients about child sexual abuse that occurred while they were in treatment was mandated. In 1989 all patient disclosures, even about such abuse that occurred before treatment, became reportable. During the period of statutory changes, the Johns Hopkins Sexual Disorders Clinic had kept track of adult patients who referred themselves for treatment and adult patients' disclosures of child sexual abuse. This allowed analysis of the impact produced by changes in the reporting requirements. Results: 1) Mandatory reporting of disclosures about prior child sexual abuse deterred undetected adult abusers from entering treatment. The rate of self-referrals when such reporting became mandatory in 1989 dropped from approximately seven per year (73 over a 10-year period) to zero. This may have caused some unidentified children to remain at risk. 2) Mandatory reporting deterred patients' disclosures about child sexual abuse that occurred during treatment. In 1988 the disclosure rate during treatment dropped from approximately 21 per year to zero. This deprived clinicians of information important for early intervention. 3) Mandatory reporting failed to increase the number of abused children identified. The number identified secondary to such disclosures was zero. Conclusions: Optimal protection of children, as well as treatment for adult patients, may be better accomplished by legislation that supports options other than reporting.

(Am J Psychiatry 1991; 148:449–453)

Two types of statutes determine whether communications between a patient and a psychiatrist must remain confidential. Statutes on privileged communications forbid a psychiatrist to disclose information without a patient's permission. Statutes on mandatory reporting require that information be divulged even if a patient objects. Mandatory reporting takes precedence over privileged communications.

In all 50 states, reporting of suspected sexual abuse of children is mandatory (1). The relevant statues were enacted because of well-intentioned concerns about protecting children, but enactment was not necessarily based on data demonstrating such statutes' effectiveness. Modifications of statutes on mandatory reporting in the state of Maryland have afforded an opportunity to assess effectiveness empirically.

One intent of this paper is to review briefly the differences between privileged communications and mandatory reporting. A second intent is to present data from Maryland that raise questions about whether mandatory reporting of suspected sexual abuse of children (which eliminates confidentiality) invariably serves its intended purpose.

PRIVILEGED COMMUNICATIONS

The Hippocratic oath states, "All that may come to my knowledge in the exercise of my profession . . . which ought not to be spread abroad I will keep secret and will never reveal." The tradition of maintaining patients' confidences is old and time-honored.

However, time-honored traditions are not synonymous with statutory protection. Therefore, historically, patients and their psychiatrists have supported efforts to codify requirements that communications be-

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tween them remain confidential. The statutory privilege belongs to the patient.

Various sorts of communications are protected by statute. These include communications between the clergy and penitents and those between attorneys and clients. In some states, even though psychiatrist-patient privilege is recognized, physician-patient privilege is not (2).

An amicus brief presented to the U.S. Supreme Court by the APA emphasized that "an effective psychotherapeutic relationship is premised on confidentiality. It is a fundamental prerequisite to successful diagnosis and treatment" (3). Analogously, the courts defined the rationale underlying attorney-client privilege: "A lawyer can act effectively only when he is fully advised of the facts and the client's knowledge that a lawyer cannot reveal his secrets promotes full disclosure" (4). Mandatory reporting, in superseding confidentiality, may make accurate diagnosis and successful treatment difficult.

Privileged communications notwithstanding, psychiatrists are ordinarily required to intercede if they know about an intended future dangerous act. Patients' disclosures about their previous acts, even those of a criminal nature, however, are ordinarily privileged.

Patient privilege is not absolute. Exceptions may occur, for example, when information must be divulged in order to place a patient in a medical facility (5). Such exceptions permit information to be divulged but do not mandate it. Communicable diseases may have to be reported, but this does not ordinarily create a conflict of interest between the patient and society.

MANDATORY REPORTING

In a free society, neither private citizens nor physicians are ordinarily compelled to act as informants for the state. It is not a crime if one exercises the prerogative not to report his or her neighbor for public intoxication. Psychiatrists are, however, required by statute to report suspected child abuse. Legislative changes were made in the requirements for reporting child abuse in Maryland in 1964, 1988, and 1989.

The first such law to be proposed in Maryland came before the legislature in 1963. Because of fears of possible civil suits against reporting psychiatrists, it was not enacted until the following year. The 1964 statute mandated reporting when suspicions of abuse emerged during clinical examination of a child. It did not mandate reporting the disclosures made by adult patients in psychotherapy (6).

In 1987 the state legislature enacted a new statute (7), which required reporting of child sexual abuse disclosed by adult patients seeking treatment or in treatment. However, the new statute allowed a three-part exclusion. Reporting was not required if 1) the suspected abuse occurred before the adult patient initially sought treatment, 2) knowledge about the abuse was derived solely from the patient's disclosures, and 3) the patient was seeking professional assistance from a program specializing in the treatment of pedophilia. The intent of the exclusion was to encourage adults whose sexual involvements with children had gone undetected to come forward so that the abuse would end. The law became effective on July 1, 1988.

This exclusion generated intense political emotion. Lay opponents labeled it the "Pedophile Protection Bill," while professional organizations such as the Maryland Psychiatric Society took no stance. There was much opinion and few data. Within a year the state legislature removed the exclusion. As of July 1, 1989, all disclosures suggesting sexual abuse of children by adult patients seeking treatment or already in treatment had to be reported. The only remaining exception was if such reporting violated aspects of attorney-client privilege.

Maryland law had been modified, then, in at least three significant ways. 1) From 1964 until 1988, sexual abuse of children disclosed by adult patients did not have to be reported. 2) As of July 1, 1988, reporting of such disclosures became mandatory, but generally only if the abuse had occurred after the adult had entered treatment. 3) As of July 1, 1989, 1 year later, disclosure of abusive behavior that occurred before the adult patient entered treatment also had to be reported.

Because of these statutory changes, it became possible to look at several issues. 1) Had these changes affected the frequency of patients' disclosures of child sexual abuse that occurred while the patients were in treatment? 2) Had the changes affected the frequency of disclosures by prospective patients about abuse that occurred before treatment? 3) Had the changes had an impact on the frequency with which adults were coming forward to report previously undetected abuse? 4) Had the changes had a positive impact on the number of child victims identified through adult patients' disclosures?

DISCLOSURE DURING TREATMENT

The Johns Hopkins Sexual Disorders Clinic, as currently constituted, has specialized in the evaluation and treatment of paraphilic disorders since 1979. Patients can receive treatment in prison, as hospital inpatients, or as outpatients in the community. Over the past several years, the number of individuals in treatment in the community at any given time has remained relatively constant, varying from approximately 180 to 220, 98% of whom are male. About 55% have diagnoses of pedophilia.

In treating patients with paraphilia and related disorders, it is crucial to document treatment outcome. Therefore, the clinic has developed a systematic method for tracking both criminal recidivism (behavior resulting in arrest) and clinical relapse (8). An initial step in that process involves recording relevant information on a standardized relapse report form. The form is divided into several sections. One section documents the initial source of the relapse report, such as a patient's disclosure during therapy. The form also documents type of abuse during the relapse (e.g., exposing, touching, intimate sexual contact, or penetration).

These data were available for much of the time during which the changes in Maryland law were taking place. Therefore, it was possible to determine what effects, if any, these changes had produced on patients' disclosures about child abuse while they were in treatment.

OUTCOME

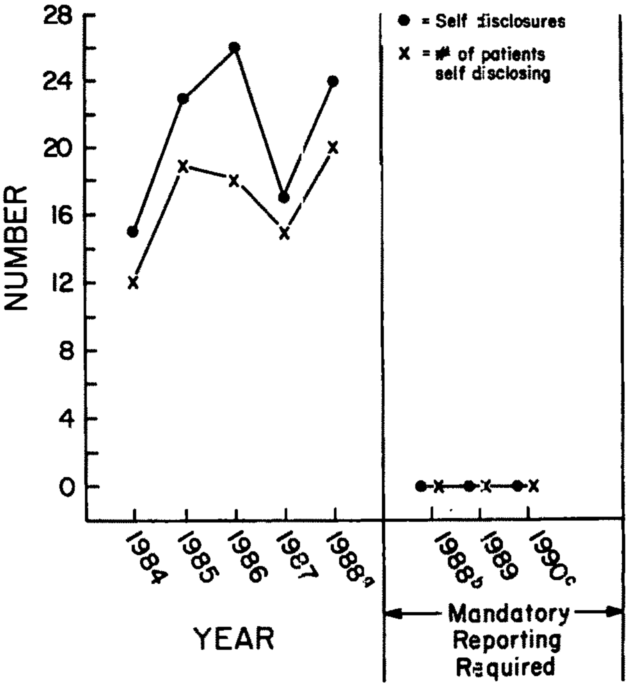
Figure 1 shows both the total number of patients who made disclosures about child abuse and the total number of these disclosures. The data are restricted to disclosures about sexual involvements with children that occurred while the adult patients were in treatment at the clinic (i.e., relapses) between 1984 and 1990. The number of disclosures exceeds the number of patients because some patients made more than one disclosure. None of the patients had been accused by others of criminal wrongdoing at the time the disclosure was made. The way in which the disclosures were dealt with clinically is discussed later in this paper.

The clinic had begun formally tracking disclosures in 1984. Between Jan. 1, 1984, and July 1, 1988, patients' disclosures regarding relapse during treatment did not have to be reported. During that time, the rate of disclosures was a little less than two per month (or about 21 per year). After July 1, 1988, when the Maryland law changed and required that such disclosures be reported, the number dropped to zero, where it has remained since. Because patients made no disclosures of relapse during treatment after the law changed, no children at risk could be identified. The rate of disclosures about offenses that did not have to be reported (e.g., those not involving children, such as voyeurism or exhibitionism) did not drop off during this time.

Analysis of the types of relapses disclosed by patients before July 1, 1988, revealed that 72% (67 of 93 disclosures) were about actions in which there was no adult-child genital contact, for example, unsuccessful propositioning of child prostitutes, voyeurism involving a child while masturbating, or touching a youngster on the thigh and being privately aware of experiencing sexual excitement. Of the 26 disclosures of genital contact, the majority (N=17) were related to fee-for-sex interactions with male adolescents. Patients making a sincere effort to succeed in treatment would be unlikely to fail initially in an extreme fashion (e.g., by engaging in intercourse with a sexually naive youngster). In this sense, the types of relapses disclosed by the patients were generally compatible with what might be expected from persons trying to succeed in treatment but struggling.

Prior to July 1, 1988, when a patient made a disclosure, a variety of clinical actions were quickly initiated. These included immediate hospitalization, voluntary removal from the home when indicated, or voluntary initiation of pharmacotherapy to suppress sexual appetite. In no instances were patients knowingly permitted to continue improper sexual activity. The availability of this type of clinical information allowed early intervention—intervention that is no longer possible in the absence of such disclosure.

FIGURE 1. Disclosures of Relapse Into Sexual Abuse of Children by Adults in Treatment at a Maryland Clinic



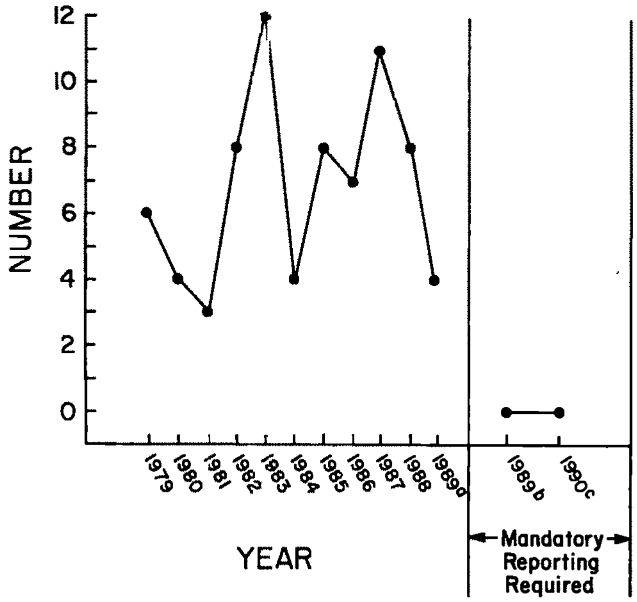
[a] Before July 1. The number for the first 6 months of 1988 was projected to a yearly rate by doubling it (projected disclosures=24, actual disclosures=12).
[b] After July 1.
[c] Before July 1.

ADULTS ENTERING TREATMENT FOR PREVIOUSLY UNDETECTED ABUSE

For approximately the past 11 years, the Johns Hopkins clinic has maintained a record of patients who have sought treatment although no criminal allegations have been made. Prior to July 1, 1989, patients whose sexual involvements with children had previously gone undetected could seek treatment without fear of criminal jeopardy. Even so, such self-referrals could be difficult. Some prospective patients probably worried that they would be reported even if the law did not require it. Indeed, this had occurred at other treatment facilities. Stigma and shame could also act as deterrents. Prospective patients may not have known where to go to find help, and denial and rationalization regarding the need for help are common.

Figure 2 shows that in spite of such difficulties, a

FIGURE 2. Self-Referred Adults Entering Treatment at a Maryland Clinic After Previously Unreported Sexual Abuse of Children (projected N=75, actual N=73)



[a]Before July 1. The number for the first 6 months of 1989 was projected to a yearly rate by doubling it.
[b]After July 1.
[c]Before July 1.

total of 73 self-referred patients who had previously engaged in some type of sexual activity involving children entered treatment at the clinic between Jan. 1, 1979, and July 1, 1989. They were not facing criminal allegations at the time they entered treatment, and none of their disclosures, to the best of our knowledge, subsequently came to the attention of criminal justice authorities. The rate of self-referrals of this sort between Jan. 1, 1979, and July 1, 1989, was approximately seven per year, or one every 2 months. A year after the law changed on July 1, 1989, not a single self-referred patient not facing criminal charges who had a previously undetected history of sexual activity with children had entered treatment.

During the first several months following implementation of the 1989 statute, clinic lawyers were of the opinion that reporting was not required if a patient was referred by an attorney for evaluation (as opposed to treatment). Prospective patients who contacted the clinic were told this. During that time period, five patients, all of whom were unknown to the criminal justice system, inquired about evaluation under attorney-client privilege. None of them, however (including four following the advice of their attorneys), was willing to enter treatment if doing so required reporting to criminal justice authorities. It is not surprising that attorneys had advised against such self-incrimination. A review of our clinical records revealed that four patients, seen previously after having disclosed their child sexual abuse elsewhere and having been reported, eventually had been sentenced to a total of 110 years in prison.

On Feb. 8, 1990, the Attorney General of Maryland gave the opinion that individuals seeking psychiatric evaluation who have not been criminally charged, even if they are referred by a lawyer, are not protected by attorney-client privilege (9). No patients with histories of previously undetected sexual involvement with children have pursued evaluation at the clinic since that time.

Persons who had referred themselves before July 1, 1989, had a variety of vocations. There was a priest who had begun nongenitally fondling boys after having been prescribed testosterone for a medical condition, an attorney fearful of disbarment if incest with his daughter were disclosed, and a schoolteacher who had nongenitally fondled students. There was also a father of several adopted children who feared that he and his wife would lose them, an adolescent counselor employed at a boys' home, a social worker who had fondled his grandchild, and a security guard who had had sexual contacts with children while employed at an art gallery. Neither they, nor in some cases their families, had been willing to identify themselves and to enter treatment before being assured that reporting to the criminal justice system was not required.

In response to clinical intervention, a number of the 73 patients who had sought treatment of their own accord gave up previous employment involving access to children. All participated in therapy, including couples therapy when indicated. A number moved out of their homes to prevent access to children. Some began treatment with medication to suppress sexual appetite.

Since the 1989 law mandating the reporting of behavior that occurred before (as well as after) seeking assistance went into effect, not a single child has been identified as a consequence of an adult's entering treatment and disclosing abuse. Much clinical information has been lost, and clinical interventions of the type just noted are no longer possible. One cannot intervene clinically if individuals who need help refrain from identifying themselves in the first place.

DISCUSSION AND CONCLUSIONS

Privileged communication statutes protect the privacy of therapy. Mandatory reporting, by superseding privilege, significantly alters the psychiatrist-patient relationship (10). Psychiatrists become informants for the state when patients incriminate themselves. Arguably, this may be necessary if a useful societal purpose is served. The data presented here suggest that this is not so.

Mandatory reporting, at least insofar as its effects on a large sexual disorders clinic are concerned, has not led to identification of even a single child at risk. At the same time, it appears to have deterred honest disclosure by patients in treatment and to have deterred unidentified potential patients from entering treatment.

This deprives clinicians of the opportunity to try to intercede constructively, and some children may therefore remain unnecessarily at risk.

The data we have presented do not address the issue of the numbers of children identified throughout the entire state of Maryland as a result of patients' disclosures of sexual abuse. It is important to do additional research exploring that matter further. The data suggest that imposing mandatory reporting on specialized clinics designed to treat adult offenders is counterproductive.

The Johns Hopkins clinic uses the informed consent procedure for patients and prospective patients. Each is told beforehand that certain types of disclosures will result in reporting. It would probably be possible to identify some children at risk by eliminating the practice of informed consent. However, this would represent a significant departure from societal expectations and a redefinition of the physician-patient relationship. In the absence of a clear declaration of legislative intent to establish such a fundamental alteration in this relationship, the clinic feels that the informed consent procedure must be followed.

Our findings suggest that children at risk were not being identified by the disclosures of adult patients regardless of whether mandatory reporting was in effect. In this sense, mandatory reporting failed to achieve its desired intent of identifying and helping abused children. The problem of identifying children could, perhaps, be resolved in some cases by eliminating mandatory reporting and treating the matter of sexual abuse of children within a mental health, rather than a criminal justice, framework. This might allow some children to be identified through adults' disclosures and to be treated, since the adults' fear of being reported to the criminal justice system would be obviated. Reporting could still be mandated for adult patients in treatment who subsequently become uncooperative.

One could argue that adults should be willing to accept punishment when they disclose child abuse. Moralizing rhetoric notwithstanding, our data suggest that this rarely occurs. Given the extreme penalties that adults who make such disclosures might have to face, it is probably unrealistic and perhaps even unreasonable to expect anything else. Ultimately, society may need to decide in some instances whether it is more important to emphasize a criminal justice approach, giving priority to prosecuting offenders, or to emphasize a public health approach, giving priority to the identification and treatment of abused children.

Some states now have statutes regarding dangerous patients in treatment (11). These statutes generally permit notification of persons at risk and of the authorities as one possible action, but not the only one. Documentation of a clinical plan that adequately addresses the well-being of others as well as the treatment of the patient can be an acceptable alternative. Although these statutes are less than ideal, they may represent a better model for dealing with the problem of child sexual abuse than does mandatory reporting.

Sexual abuse of children is an upsetting and emotional issue. The problem cannot be solved, however, by outrage, polarization, or less than adequate legislation. It is not caused by children but by the adults who pose a risk to them. Many such adults are themselves former victims (*DSM-III-R*, p. 285, and 12). Adequate resolution and prevention of this problem require the provision of effective mental health services to both adults and youngsters. They also require a climate of opinion that does not create a conflict of interest between children and adult patients, that does not see their interests as mutually exclusive but, rather, as complementary, and that accepts the legitimacy of regarding adults who disclose sexual abuse as patients.

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An Empirical Study of Diagnostic Criteria for Delirium

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Objective: The objective of this study was to determine empirically how many patients are identified as delirious or nondelirious according to DSM-III, DSM-III-R, *and* ICD-10 *criteria. Method: Daily, a trained research assistant using a structured instrument to detect the presence of symptoms of delirium evaluated 325 elderly patients who were admitted to a general hospital for acute medical problems. Each patient's symptoms were then compared with these diagnostic criteria sets to determine if the patient met criteria for delirium. Results:* DSM-III *criteria were the most inclusive: they identified 125 patients as delirious.* DSM-III-R *identified a somewhat different group of 106 patients as delirious.* ICD-10 *criteria identified only 30 patients as delirious. Conclusions: The development of new criteria for delirium (e.g.,* DSM-IV*) will have to balance the need to define a pure group of patients for research purposes with the need to include cases of clinical interest. Changes in criteria should be based on data such as those presented in this paper.*

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Delirium as a diagnostic entity presents some special problems in current classification schemes. Although no specific criteria for delirium exist in *ICD-9, DSM-III* did include specific criteria. These criteria were based on extensive clinical experience, particularly that of general hospital psychiatrists. Lipowski (1) described the core features of the syndrome as "disorders of cognition, attention, sleep-wake cycle, and psychomotor behavior" but pointed out that "studies of the phenomenology of delirium in old age are almost nonexistent." Despite the absence of phenomenological studies of delirium, *DSM-III-R* contained a substantial revision of the criteria for delirium. A major difference was the addition of "disorganized thinking, as indicated by rambling, irrelevant, or incoherent speech" as a necessary or required criterion for making the diagnosis. The clouding of consciousness that was required in *DSM-III* was redefined as a reduced level of consciousness and became one of six criteria of which at least two had to be present. Disorientation and memory impairment were also no longer absolutely required, as they had been in *DSM-III,* but were among these six criteria. These changes were all made after extensive discussion but without data from field testing or clinical research. *ICD-10* is also being developed by consensus; the clinical version has no specific criteria. In addition, research criteria have been proposed for *ICD-10* that are more extensive than those in *DSM-III-R.*

This paper will summarize the relevant literature, compare the *DSM-III, DSM-III-R,* and *ICD-10* proposed research criteria by using data from a large study of delirium in hospitalized elderly patients, identify problems with the criteria, and suggest considerations for revisions of the criteria. These data may help inform the development of *DSM-IV* criteria (2).

LITERATURE REVIEW

Most of the published literature consists of reviews of the clinical syndrome of delirium (1, 3–10). Other papers (11–15) reported cases of "delirium" (not always explicitly defined) due to various causes and reported different characteristics of patients with delirium. Some studies have examined the consequences of delirium, including mortality (16), length of hospital stay (17), or both (18).

The papers cited clearly indicated that delirium is a frequent and serious clinical problem in hospitalized elderly patients and that it is often unrecognized. However, none of these papers directly addressed the questions of how valid and how reliable the diagnostic cri-

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teria in *DSM-III, DSM-III-R,* or *ICD-10* are. One study that attempted to test the *DSM-III* criteria for delirium in medical inpatients (19) reported that "delirium could be readily and reliably detected using the *DSM-III* criteria." However, the authors did not describe how they trained their observers to rate each symptom or whether the diagnosis was made on a more global impression. The authors also noted that *DSM-III* criteria do not include operational definitions of symptoms such as clouding of consciousness. Trzepacz et al. (20) developed a rating scale for delirium based on clinical observations. To date, no subsequent studies have been published using their Delirium Rating Scale. *DSM-III-R* attempted to address the issue of operationalizing the criteria by including specific examples. For instance, the criterion of reduced level of consciousness is accompanied by the example, "difficulty keeping awake during examination." However, other criteria, such as "increased or decreased psychomotor activity," do not include specific behaviors to be observed and rated. Johnson et al. (21) operationalized *DSM-III* criteria; a psychiatrist then applied these criteria to a group of 235 elderly patients admitted to a general hospital medical service.

METHOD

In the present study, elderly hospitalized patients were rated on the presence of symptoms in each domain of *DSM-III* delirium (clouding of consciousness, disorientation and memory impairment, perceptual disturbance, incoherent speech, increase or decrease in psychomotor behavior, disturbance of sleep-wakefulness cycle, and fluctuating clinical features). Since the study involved daily assessments of a large number of patients over their entire hospital stay, it was impractical to have a clinician conduct all the assessments. Therefore, an interdisciplinary group developed an instrument (the Delirium Symptom Interview) that described the behaviors or responses associated with a particular symptom in explicit, operational terms so that a research assistant could perform the assessments. An extensive training manual was developed that provided very specific definitions and instructions for a nonclinician on how to interpret and rate particular behaviors. This produced excellent interrater reliability between two research assistants. The instrument was also field-tested in 50 elderly hospitalized patients and found to have good agreement with the symptom ratings done by a trained neurologist (D.M.P.) and a trained psychiatrist (B.L.), both of whom were experienced and expert in the care of the elderly (22).

Using data collected as part of our unpublished prospective study of delirium in hospitalized elderly patients, we compared the number of patients diagnosed as delirious according to *DSM-III, DSM-III-R,* or proposed *ICD-10* research criteria. Two groups of elderly patients who were admitted to Beth Israel Hospital for medical or surgical care were studied, one from a defined community and the other from a long-term-care facility. Patients admitted to an intensive care unit were excluded. The data from this study are unique because data on symptoms were collected without requiring that patients meet *DSM-III* or *DSM-III-R* criteria. This study also has the important advantage of not excluding patients with dementia. The Delirium Symptom Interview was used to rate symptoms of delirium so that diagnoses could be arrived at retrospectively by using any combination of symptoms rated.

To operationalize the criteria, some decisions had to made about terms that were vague. For example, the *DSM-III* requirement that "clinical features . . . develop over a short period of time (usually hours to days) and tend to fluctuate over the course of a day" was addressed by defining symptoms as new if they were not present when the patient was first seen or, if present, were symptoms that relatives or caretakers reported had not been present before the hospitalization. None of the criteria sets included specific instructions for what time period should be considered for symptoms to coexist. The definition we used required that all symptoms be present within the same 24-hour period. Fluctuating behavior was rated but was not required for *DSM-III* or *DSM-III-R* definitions. Criterion E from *DSM-III* and *DSM-III-R* and criterion G from *ICD-10* were addressed in general terms because in most cases a specific etiologic factor could not be identified (18). No patients in the present study were diagnosed as having a functional disorder, and all were physically sick enough to be admitted to a general hospital; therefore, organic conditions could be presumed.

RESULTS

Table 1 compares the patients who met *DSM-III* criteria with the overlapping groups of patients who met *DSM-III-R* criteria and *ICD-10* research criteria for delirium.

Of the 325 patients seen, 125 (38%) met *DSM-III* criteria for delirium, 106 (33%) met *DSM-III-R* criteria, and 30 (9%) met *ICD-10* research criteria for delirium. Of the 125 patients who met *DSM-III* criteria, 26 did not meet *DSM-III-R* criteria. This difference was accounted for, in part, by seven patients who spoke very little and could not be rated on the *DSM-III-R* criterion of disorganized thinking and by seven patients who had all the symptoms of *DSM-III-R* delirium at some point during their hospitalization but not all within the same 24-hour period. Seven of the 104 patients who met *DSM-III-R* criteria did not meet *DSM-III* criteria. Four patients were not disoriented and four experienced the disturbance of consciousness for only 1 day and not within the same 24-hour period as the other required symptoms. One hundred two patients who met either *DSM-III* or *DSM-III-R* criteria did not meet *ICD-10* criteria: 37 of these patients had the required symptoms but not in the same 24-hour

TABLE 1. Characteristics of Hospitalized Elderly Medical Patients Who Met *DSM-III*, *DSM-III-R*, or *ICD-10* Research Criteria for Delirium

Delirium Status	Age (years)		Length of Stay (days)		In-Hospital Mortality		Mortality 6 Months After Discharge	
	Mean	SD	Mean	SD	N	%	N	%
Met *DSM-III* criteria (N=125)	86	6	19	27	7	6	29	23
Met *DSM-III-R* criteria (N=106)	86	6	20	29	6	6	24	23
Met *ICD-10* criteria (N=30)	87	7	20	31	2	7	7	23
Total study group (N=325)[a]	81	8	12	19	9	3	55	17

[a]The total study group includes all patients regardless of whether they met any criteria for delirium.

period, 49 patients did not meet criterion B because they did not have three global disturbances of cognition, an additional six patients were missing a new sleep disorder, eight were missing a psychomotor symptom, and two were missing both a new sleep disorder and a psychomotor symptom.

The three overlapping groups of patients were virtually identical in mean age, mean length of stay, and mortality rates (see table 1).

DISCUSSION

Of the three criteria sets considered in this study, *DSM-III* criteria are the most inclusive and *ICD-10* proposed research criteria are the most restrictive. *DSM-III-R* and *ICD-10* criteria exclude many patients whom most clinicians would diagnose as having delirium. Some of the difference in the detection rates for delirium could be reduced by requiring that all of the symptoms exist in the same 72-hour period rather than the same 24-hour period we required. Similarly, the seven patients in our study who met *DSM-III* but not *DSM-III-R* criteria because their sparse speech made it impossible to judge whether their thinking was disorganized could be included as having delirium by adding the phrase "if testable" after the criterion of disorganized thinking. Although whether disorganized thinking is necessary for making a diagnosis of delirium is a conceptual decision, the data here suggest that some of the patients in our study would be clinically diagnosed as delirious without this symptom. In addition, the majority of the patients who met *DSM-III* or *DSM-III-R* criteria did not have enough symptoms to meet the proposed *ICD-10* research criteria. These criteria are so detailed that they are overly restrictive. They are highly specific but not very sensitive—that is, they lead to few false positives but many false negatives.

Other issues emerged in the development of our rating instrument. Some of the criteria are inherently problematic to rate. For example, insomnia is very difficult to judge in a general hospital population because patients are often awake because they are in pain or having trouble breathing or because nursing interventions disrupt their sleep. Conversely, they might be given a hypnotic drug to help them sleep through the night. Hypnotic drugs, trouble breathing, and disrupted sleep may cause delirium but do not necessarily indicate the presence of delirium. Similarly, psychomotor activity may be decreased because patients are physically ill and confined to bed rather than because they are delirious. Rating speech as rambling, irrelevant, or incoherent may be impossible in a patient who is ill or hearing impaired and who does not produce much speech. It is difficult to know how to use or rate the requirement that "clinical features develop over a short period of time (usually hours to days) and tend to fluctuate over the course of a day." What if some features fluctuate but others are preexisting or are more consistently present even over long periods? In rating disorientation or memory impairment there are no specific directions in any of the criteria sets as to whether to count these symptoms as positive if they are caused by an underlying dementia. If they are counted as positive, the rate of delirium would clearly be higher in demented patients because they already met some of the criteria. This raises the whole issue of the overlap of symptoms of dementia with those of delirium.

Another problem with the three sets of criteria is the requirement for a specific etiological factor. In many or most cases, it is impossible to implicate any individual factor when a patient has multiple physical impairments and is receiving multiple medications (18). Furthermore, some patients with functional disorders such as mania are delirious, and it is important to document the presence of delirium in addition to the manic symptoms.

Based on these findings, several options are available for future criteria (*DSM-IV*, for instance). One would be to keep the present *DSM-III-R* criteria for clinicians and investigators who are just now becoming familiar with them. This strategy would preserve the specific examples that begin to operationalize the criteria. The disadvantage in this approach is that the *DSM-III-R* criteria clearly miss a substantial number of patients whom most clinicians would classify as having delirium. A return to the *DSM-III* criteria, with the addition of some examples to help operationalize the criteria, would not be too disruptive because most clinicians are already familiar with them. The minor criteria, such as sleep disturbance and psychomotor retardation, could be considered associated features rather than necessary for the diagnosis of delirium because they are heavily confounded in a hospital setting for reasons given in this paper. The requirement for a specific etiological factor or the absence of another psychiatric disorder could be dropped for the reasons already given.

Any new criteria developed should be incorporated in both *DSM-IV* and *ICD-10* (23). Explicit criteria could be eliminated, as they are in the draft clinical criteria of *ICD-10* (not the research criteria), since this would recognize the paucity of available data and would provide the most opportunity for ongoing phenomenological research into the syndrome of delirium. However, this approach would provide no guidance to clinicians or investigators in defining the syndrome of delirium and would be a step backward from the overall thrust of *DSM* toward use of explicit diagnostic criteria. By not clearly describing the syndrome, it could perpetuate the underdiagnosis of delirium by physicians and nurses who might have too restrictive a definition or one that focuses on a particular subtype, namely, the hyperactive, agitated, or hallucinating delirious patient. Continued research is clearly needed to better define the syndrome of delirium.

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Diagnosing Dissociative Disorders in The Netherlands: A Pilot Study With the Structured Clinical Interview for DSM-III-R Dissociative Disorders

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Objective: To improve the ability to diagnose dissociative disorders in The Netherlands, the authors conducted a study using a Dutch version of the Structured Clinical Interview for DSM-III-R Dissociative Disorders (SCID-D) with additional questions on childhood trauma and symptoms of borderline and histrionic personality disorders. Method: All interviews were audiotaped or videotaped and rated by two investigators separately. Forty-four patients (42 women and two men) participated in the study. Most of the patients had been referred for evaluation of dissociative symptoms; five had participated in a nationwide survey on incest. None of the patients had ever received a diagnosis of a dissociative disorder, and none had evidence of organic brain syndrome or mental retardation. All patients were in active treatment: 23 were being treated in an outpatient psychiatric service, 13 in an inpatient psychiatric service, and eight in private practice. Thirty-two patients had been psychiatric inpatients at least once. Results: Four diagnostic groups of patients were identified: two with dissociative disorders (12 patients with multiple personality disorder and 11 with dissociative disorder not otherwise specified), one with DSM-III-R *personality disorders (11 patients), and one without dissociative or personality disorders (10 patients). Conclusions: Dissociative disorders are clearly not only an American phenomenon. The diagnosis can be made outside of the United States if the symptoms are sought. The SCID-D proved to be a promising instrument.*

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Despite the original contributions of French psychiatry in the nineteenth century (1), dissociative disorders have been neglected in European psychiatry. Major developments in diagnosis and treatment of dissociative disorders in the last decade stem from North America, where in 1980 APA classified the dissociative disorders as a new diagnostic category. In *DSM-III-R* the dissociative disorders are listed as multiple personality disorder, psychogenic fugue, psychogenic amnesia, depersonalization disorder, and dissociative disorder not otherwise specified. Multiple personality disorder has been the most thoroughly investigated of these disorders in the past 10 years. There have been few recent clinical studies on the other *DSM-III-R* dissociative disorders, however (2).

Dissociative symptoms are not confined to dissociative disorders. These symptoms have been documented in general and specific disorders among psychiatric patients, particularly in patients with posttraumatic stress disorder (PTSD) (3), eating disorders (4), borderline personality disorder (5), and hysterical psychosis (6).

Outside the United States there is much skepticism and ambivalence about dissociative disorders as a distinct diagnostic category and especially about the validity of the diagnosis of multiple personality disorder. Articles in the *British Journal of Psychiatry* reflect this attitude, suggesting that multiple personality disorder is a culture-bound phenomenon specific to North America (7–9).

In The Netherlands, interest in the field of dissociative disorders is growing; cases of multiple personality disorder and other dissociative disorders are reported more often, and the relationship between multiple personality disorder and childhood trauma is recognized (10, 11). More solid research is needed, however, to

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develop a cross-culturally valid and reliable procedure to assess dissociative symptoms and disorders.

DIAGNOSTIC INSTRUMENTS

Recently, two structured interviews for dissociative disorders—the Dissociative Disorders Interview Schedule (12) and the Structured Clinical Interview for DSM-III-R Dissociative Disorders (SCID-D) (13)—have been developed. Before beginning this study we compared these instruments.

The Dissociative Disorders Interview Schedule is a highly structured interview for *DSM-III-R* dissociative disorders, somatization disorder, major depressive episode, and borderline personality disorder. Although the Dissociative Disorders Interview Schedule has been used in several studies to compare features of patients with multiple personality disorder with those of other diagnostic groups, only limited data on reliability (based on 10 patients with multiple personality disorder) and validity have been published (12).

The SCID-D is a semistructured diagnostic interview for the assessment of *DSM-III-R* dissociative disorders. Five dissociative symptom areas—amnesia, depersonalization, derealization, identity confusion, and identity alteration—are evaluated in order to reach *DSM-III-R* dissociative disorder diagnoses. In a preliminary study (13), reliability rates were almost uniformly in the good (0.60) to excellent (0.95) range, and the SCID-D discriminated significantly in all assessments among patients with dissociative disorders, patients with nondissociative disorders, and normal control subjects. The SCID-D is able to assess separately the severity of dissociative symptoms, which is extremely useful and makes it a good instrument for research on dissociative symptoms among different clinical populations. For these reasons we chose to introduce the SCID-D in The Netherlands.

METHOD

The SCID-D was translated from English into Dutch; this translation was checked by bilingual clinicians. Initial interviews were conducted to become acquainted with the instrument and to check the flow of the interview. We consulted with M. Steinberg, who developed the instrument, and were given 2 days of training.

In addition to the SCID-D we developed a structured interview on childhood and adult sexual and physical traumata and related symptoms (self-mutilation, suicidality, eating disorders, and PTSD, among others), as well as symptoms of borderline personality disorder and histrionic personality disorder. This part of the interview was administered after the SCID-D.

All interviews were audiotaped or videotaped and rated by the two of us separately. Informed consent, including consent to video- and audiotaping, was obtained from all patients.

Forty-four patients (42 women and two men) participated in this study. Most of the patients had been referred for evaluation of dissociative symptoms; five had participated in a nationwide survey on incest (14). None of the patients had ever received a diagnosis of a dissociative disorder, and none had any evidence of organic brain syndrome or mental retardation.

All of the patients were in active treatment: 23 were being treated in an outpatient psychiatric service, 13 in an inpatient psychiatric service, and eight in private practice. Thirty-two patients had been psychiatric inpatients at least once.

The mean age of the patients was 32.6 years (range= 18–53). Only 11 patients were currently employed; the rest were receiving disability payments.

RESULTS

Interrater reliability for absence or presence of *DSM-III-R* dissociative disorder and type of dissociative disorder was assessed. Of the 44 patients, the diagnosis of dissociative disorder was assigned independently to 22 patients by one of us and to 23 by the other (there was agreement on the absence or presence of a dissociative disorder in 43 [97.7%] of the 44 cases).

Twelve of the 23 patients with dissociative disorders met the criteria for multiple personality disorder (there was 100% agreement on this diagnosis). The diagnosis of dissociative disorder not otherwise specified was given to 10 of the 23 patients by one of us and to 11 patients by the other. After discussion the one patient on whom we disagreed was given the diagnosis of dissociative disorder not otherwise specified because of the severity of the patient's dissociative symptoms.

No patients with diagnoses of psychogenic amnesia, psychogenic fugue, or depersonalization disorder were identified. All patients with psychogenic amnesia or fugue met criteria for multiple personality disorder or dissociative disorder not otherwise specified.

The patients without dissociative disorders were subdivided into two groups: one group (11 patients) met criteria for personality disorders and the other group (10 patients) did not (table 1).

Of the 23 patients with dissociative disorders, nine (39%) also met *DSM-III-R* criteria for personality disorders: eight patients met criteria for borderline personality disorder and one patient met criteria for histrionic personality disorder. In the further analysis of dissociative symptoms, four groups were compared: two with dissociative disorders (12 patients with multiple personality disorder and 11 with dissociative disorder not otherwise specified), one with *DSM-III-R* personality disorders (11 patients), and one without dissociative or personality disorders (10 patients).

The groups did not differ in age or level of education. Patients without dissociative disorder or personality disorder differed strikingly from the other pa-

TABLE 1. Scores for Symptoms on the SCID-D[a] for Four Diagnostic Groups of Patients Referred for Dissociative Symptoms

	No Dissociative Disorder				Dissociative Disorder			
	No Personality Disorder (N=10)		Personality Disorder (N=11)		Dissociative Disorder Not Otherwise Specified (N=11)		Multiple Personality Disorder (N=12)	
Symptom	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Amnesia	1.3	0.48	2.10	0.32	3.45	0.82	4.00	0.00
Depersonalization	2.0	1.05	3.36	0.50	3.55	0.69	3.75	0.45
Derealization	1.3	0.48	1.73	0.65	1.64	0.81	2.50	1.17
Identity confusion	1.6	0.84	2.27	1.01	3.27	1.01	3.92	0.29
Identity alteration	1.0	0.00	1.45	0.82	3.00	1.18	4.00	0.00
Total SCID-D score	7.2	1.69	10.73	0.90	14.91	2.26	18.17	1.53

[a] 1=absent, 2=mild, 3=moderate, 4=severe; range of the total SCID-D score=5–20.

tients, however, in employment status: most of them were currently employed. Only one of the patients without dissociative disorder or personality disorder had a history of psychiatric disorder; the rest of this group were in treatment for neurotic problems mainly. In the three other groups only one patient was currently employed. All of the patients in these three groups had long psychiatric histories.

Analysis of variance (ANOVA, two-tailed) was used to test the significance of differences in severity of the dissociative symptoms among the four groups (table 1). Each of the five SCID-D symptoms (amnesia, depersonalization, derealization, identity confusion, and identity alteration) is scored on a 4-point scale (1=absent, 2=mild, 3=moderate, and 4=severe). The main criteria are frequency and persistence of the symptoms. The total SCID-D score ranges between 5 and 20.

The overall ANOVA results showed a significant difference among the groups (table 1). The differences between the total scores of the patients with personality disorders and those with dissociative disorders were also statistically significant (table 1). The groups differed significantly in amnesia scores. Patients with multiple personality disorder showed persistent episodes of amnesia, memory gaps lasting from hours to days, specific blocks of time that could not be accounted for, or fugue states—finding oneself in unfamiliar surroundings. The patients in the group with unspecified dissociative disorder mentioned recurrent to persistent memory dysfunctions comparable to those of the patients with multiple personality disorder. The patients with personality disorders showed amnesia in a mild form—occasional memory difficulties closely linked with the experience of depersonalization. No fugue states or specific blocks of time missing were mentioned. Patients without personality or dissociative disorders mentioned occasional forgetfulness associated with a specific stressful event. Amnesia turned out to be the most discriminating factor among the four groups.

Although the four groups differed significantly in depersonalization, closer inspection shows that this symptom did not differentiate the patients with personality disorders from those with dissociative disorders. The patients' descriptions of experiences of depersonalization differed, however. In the group of patients with dissociative disorders, questions about depersonalization typically triggered answers about identity alteration. These patients often described feelings of estrangement as if someone else inside were in charge of their behavior. They observed themselves from a point outside of their body while performing tasks or doing things they thought they could not do. They heard their own voices talking as if they belonged to someone else. The patients with personality disorders, by contrast, gave less specific descriptions: feelings of being in a haze, not being in touch with their bodies, or feeling like a robot.

Only slight differences were found among the groups in the severity of derealization. The patients with multiple personality disorder mentioned few recurrent episodes in which a change in perception of the environment took place or they occasionally did not recognize friends or family. For these patients, experiences of derealization were often associated with flashbacks or age-regressed states during which they relived traumatic experiences. Derealization was infrequently present in the other groups. There was no significant difference between the patients with personality disorders and those with dissociative disorders in derealization.

As could be expected, identity confusion was present in the patients with personality disorders and those with dissociative disorders. However, it was clearly more severe among the patients with dissociative disorders (table 1). Patients with multiple personality disorder mentioned persistent internal struggles or uncertainty as to who they were. These struggles were often described as ongoing dialogues inside their heads—different voices arguing with each other. Among the patients with dissociative disorders, identity confusion was typically linked to behaviors during amnestic episodes. Identity confusion in the patients with personality disorder was described as a recurrent struggle between a constructive and a destructive part of the self: "good versus bad" or "devil versus angel." These pa-

TABLE 1. (continued)

Difference Among All Groups (df=3, 40)		Personality Disorder Versus Dissociative Disorder (df=1, 32)		Personality Disorder Versus Multiple Personality Disorder (df=1, 21)	
F	p<	t	p<	t	p<
66.01	0.0001	7.89	0.0001	20.92	0.0001
13.41	0.0001	1.42	n.s.	1.94	n.s.
4.18	0.05	1.01	n.s.	1.94	n.s.
16.79	0.0001	4.24	0.0001	5.42	0.0001
41.21	0.0001	6.20	0.0001	10.77	0.0001
91.05	0.0001	7.52	0.0001	14.04	0.0001

tients did not hear dialogues between these elements in their heads. The patients without personality or dissociative disorders had a very low mean score on identity confusion.

Identity alteration turned out to be highly discriminative among these four diagnostic groups. The patients with multiple personality disorder had histories of identity alteration that was completely out of their control. They were referred to by different names, showed consistent behavior and social relations connected to those names in different situations, and had different abilities or talents. In all cases the patient was at least partly amnestic for behaviors of different parts of the self. The patients with unspecified dissociative disorder mentioned subtle cues of alterations in identity without enough proof of the existence of alter-personalities. Identity alteration was almost absent from the patients with personality disorders. Loss of control over one's behavior in this group was either split-off aggressive behavior among the patients with borderline personality disorder or being carried away by role-playing among the patients with histrionic personality disorder (the roles were experienced as ego syntonic). If a good and a bad part of the self were mentioned, these parts did not have different names or histories. Nor was amnesia connected with the good-versus-bad split, although responsibility for aggressive outbursts could be denied. Identity alteration was absent from the patients without personality or dissociative disorders.

Histories of severe physical abuse and sexual abuse were reported by nine of the 12 patients with multiple personality disorder; the other three patients were totally amnestic for their childhood. Four of the 11 patients with unspecified dissociative disorders mentioned complete amnesia for childhood; the other seven patients had been sexually and physically abused, five severely.

Amnesia for childhood was not mentioned by the patients with personality disorders. Four of these 11 patients had experienced severe sexual abuse, and eight had been severely physically abused.

None of the patients without personality or dissociative disorders reported severe sexual or physical abuse.

The main differences in childhood sexual and physical abuse between the patients with dissociative disorders and those with personality disorders were in the prevalence and severity of sexual abuse and in the presence of massive childhood amnesia in the patients with dissociative disorders.

Self-mutilation was found in six of the 11 patients with personality disorders, in seven of 11 patients with unspecified dissociative disorder, and in 10 of 12 patients with multiple personality disorder. Self-destructive behavior was associated with amnesia in the group of patients with dissociative disorders. No differences were found in suicidality between the patients with personality disorders and those with unspecified dissociative disorder and multiple personality disorder: nine of the 11 patients with personality disorders, seven of the 11 patients with unspecified dissociative disorder, and 11 of the 12 patients with multiple personality disorder reported recurrent suicide attempts.

DISCUSSION

In this study the SCID-D was used to identify cases of dissociative disorders that had never been diagnosed as such. All of the patients had dissociative symptoms to some extent.

Dissociative disorders share many features in common with other psychiatric disorders. One question concerns the differential diagnosis of dissociative disorders from related emotional disorders such as borderline or histrionic personality disorder.

The results of this study show that the SCID-D is a reliable diagnostic instrument to evaluate dissociative symptoms and make the diagnosis of a dissociative disorder. We found that patients with dissociative disorders differed significantly in severity of dissociative symptoms from patients without dissociative disorders. This confirms the results of the preliminary report on the SCID-D by Steinberg et al. (13). Like Steinberg et al., we found differences in severity and in clustering of dissociative symptoms.

It was also possible to discriminate between patients with dissociative disorders and patients with personality disorders, even though these two groups had many overlapping characteristics and some of the patients with dissociative disorders met criteria for personality disorders as well.

We identified no cases of psychogenic amnesia, psychogenic fugue, or depersonalization disorder. Fugues and amnestic episodes were part of another dissociative disorder (either unspecified dissociative disorder or multiple personality disorder). Although all of the patients with personality disorders met criteria for depersonalization disorder, this diagnosis was not given because depersonalization was primarily seen as a symptom of a personality disorder (*DSM-III-R*, p. 276).

Braun (15) suggested that criteria for the diagnosis of multiple personality disorder should be observed on more than one occasion to establish consistency over time before the formal diagnosis of multiple personality disorder is made. Since the multiple personality disorder of all of our patients with this diagnosis had never been detected, we gathered follow-up data on these patients. At 1-year follow-up, all diagnoses were independently confirmed and dissociative symptoms and alter-personalities were still present.

Of interest is the comparison between patients with multiple personality disorder and those with personality disorders. Overlap of symptoms between these groups was expected both on theoretical as well as empirical grounds. These patients did not differ in severity of psychiatric history, almost all of the patients in both groups were receiving welfare, almost all had had at least one previous psychiatric hospitalization, and almost all reported recurrent suicide attempts and self-mutilative behavior. However, patients with multiple personality disorder were often amnestic for their self-destructive behavior and patients with borderline personality disorder were not. Two dissociative symptoms—depersonalization and derealization—did not discriminate between patients with multiple personality disorder and those with borderline personality disorder. Amnesia, identity confusion, and identity alteration did discriminate between these two groups. Moreover, all of the patients with multiple personality disorder reported auditory hallucinations, but none of the patients with borderline personality disorder did.

Both groups reported sexual or physical trauma in childhood, but sexual abuse was more prevalent and more severe in the patients with multiple personality disorder. Our group of patients was too small to allow conclusions at this point. It is also select in that all of the patients were referred to us for evaluation of dissociative symptoms. The relation between dissociative disorders and trauma has been extensively documented (16, 17). There is some empirical evidence of a relation between borderline personality and trauma. The severity of dissociative symptoms in patients with borderline personality disorder has been found to be related to the severity of a trauma history in childhood (18). This relationship may partly explain the presence of severe depersonalization in almost all of the patients with personality disorders in our study group.

Our findings confirm results of other studies about the differential diagnosis of multiple personality disorder from borderline personality disorder: although there are many overlapping symptoms, the two disorders can be distinguished (19, 20).

Although this study has the limitation of small group sizes, we can conclude that dissociative disorders—particularly multiple personality disorder—are not culture-bound North American phenomena but are still neglected in European psychiatry and can go unrecognized. The diagnosis can be made if the dissociative symptoms are carefully assessed. All of the patients in our study who met criteria for dissociative disorders told us that they had never been asked questions about dissociative symptoms, even though most of them had long psychiatric histories. European clinicians must become more acquainted with dissociative symptoms so that patients with dissociative disorders will receive proper treatment for their problems rather than spending years in the mental health system without such treatment.

The SCID-D proved to be a good instrument for the assessment of dissociative symptoms and disorders. A controlled study using the SCID-D with a larger group of patients is currently underway.

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DSM-IV: A Nosology Sold Before Its Time?

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Objective: *The purpose of this study was to determine whether American psychiatrists believe that* DSM-IV *is being published too soon after* DSM-III-R. Method: *The authors conducted a mail survey of the attitudes of practicing psychiatrists (N=454), residency program directors (N=128), residents (N=1,331), and researchers (N=196) toward the scheduled publication of* DSM-IV *in the early 1990s.* Results: *They found that the majority of all four groups believed that* DSM-IV *is being published prematurely. In contrast to respondents who believed that the timing of* DSM-IV *is appropriate, those who indicated that it is being published too soon had more recently completed their residency training and also believed that* DSM-III-R *was published prematurely. There was no association between the psychiatrists' responses and their theoretical orientation, Board certification status, ownership of the* DSM *manuals, the length of time they had used* DSM-III, *and the diagnostic manual (*DSM-III *or* DSM-III-R*) they were currently using.* Conclusions: *The belief that* DSM-IV *is being published too soon could contribute to underuse of* DSM-IV *by substantial numbers of psychiatrists. Thus, to foster compliance with it, APA must persevere in its efforts to demonstrate that the advantages of publishing it in 1993 outweigh the disadvantages of adopting yet another manual.*

(Am J Psychiatry 1991; 148:463–467)

DSM-IV is scheduled for publication in 1993 (1), 6 years after the publication of *DSM-III-R* (which was published 7 years after *DSM-III*) (2). Zimmerman (3) argued that adherence to the projected timetable will result in *DSM-IV* being published too soon, and he described multiple problems that might result from this rapid publication schedule. Frances et al. (1) noted that one factor to be considered in the decision to revise diagnostic criteria for *DSM-IV* will be the opinions of clinicians surveyed regarding the proposed changes. We took this idea one step further and conducted a nationwide survey of American psychiatrists regarding their attitudes toward the various *DSM* versions and the issue of whether *DSM-IV* is being published too soon.

In the present report we focus on the proposed publication of *DSM-IV* in particular and the publication of new editions of *DSM* in general. We present the results of an opinion poll about the projected *DSM-IV* publication date and examine the association between survey results and respondents' background characteristics such as theoretical orientation, type of professional activity, and years of experience. In addition, we examine whether opinion about the publication of *DSM-III-R* is associated with attitudes toward *DSM-IV*. Finally, psychiatrists who indicated that *DSM-IV* is being published too soon were asked when it should be published, and all subjects were asked to recommend a general guideline for the number of years that should separate *DSM* editions.

METHOD

We surveyed four nonoverlapping groups: a random sample of 1,000 practicing psychiatrists from the American Medical Association database (practitioners' sample), the directors of all approved psychiatry residency training programs in the United States (N=198), residents in their third or fourth year of training at these programs (N=2,470), and first authors of all articles published in the *Archives of General Psychiatry* and the *American Journal of Psychiatry* in 1987 and 1988 who were physicians and to whom reprint requests were directed at a U.S. address (N=337). We

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TABLE 1. Characteristics of Practicing Psychiatrists, Researchers, and Residents Who Responded to a Questionnaire About *DSM-IV*

	Practicing Psychiatrists (N=454)[a]		Researchers (N=196)[b]		Residents (N=1,331)[c]	
Item	N	%	N	%	N	%
Sex						
Male	374	82.6	171	87.2	791	59.6
Female	79	17.4	25	12.8	536	40.4
Geographic region						
South	81	18.2	15	7.9	298	22.7
West	116	26.1	30	15.8	254	19.3
North central	97	21.8	35	18.4	307	23.4
Northeast	151	33.9	110	57.9	454	34.6
Country of medical school education						
United States	347	76.9	173	88.3	1,069	80.7
Other	104	23.1	23	11.7	256	19.3
Philosophical emphasis of practice						
Psychodynamic	127	28.2	22	11.3		
Biologic	150	33.3	97	49.7		
Eclectic	155	34.4	65	33.3		
Other	18	4.0	11	5.6		
Primary professional activities[d]						
Administration	58	12.8	68	35.1		
Teaching	72	15.9	87	44.8		
Private practice	290	64.2	39	20.1		
Research	33	7.3	128	66.0		
Salaried clinical practice	164	36.3	33	17.0		

[a] Data missing for sex (N=1), geographic region (N=9), country of medical school education (N=3), philosophical emphasis of practice (N=4), and primary professional activities (N=2).
[b] Data missing for geographic region (N=6), philosophical emphasis of practice (N=1), and primary professional activities (N=2).
[c] Data missing for sex (N=4), geographic region (N=18), and country of medical school education (N=6).
[d] Percentages total more than 100 because some respondents indicated more than one activity.

included the last group because we were interested in comparing the responses of researchers and nonresearchers, and a previous random survey of practicing psychiatrists (4) found that less than 10% identified research as one of their primary professional activities. Respondents were not included in more than one group, and, when necessary, they were hierarchically assigned to the residency director, researcher, and random sample groups.

A questionnaire was mailed to the subjects (or distributed to the residents by the program director) and was accompanied by a preaddressed, prepaid return envelope and a letter that explained the study's purpose and assured anonymity.

The four-page, 34-item questionnaires completed by the researchers, residents, and random sample of practicing psychiatrists were essentially identical. The first nine questions assessed background information such as the respondent's age, sex, theoretical orientation, type of professional activity, and year of residency completion. The remaining questions covered the training in, use of, and opinions about *DSM-III*, *DSM-III-R*, and *DSM-IV*. Residency directors completed a 23-item, three-page questionnaire that did not contain the personal background questions and that worded the questions regarding the training in and use of *DSM-III* and *DSM-III-R* to apply to the residency program rather than personal use.

There were two mailings to the researchers, residents, and random sample of practicing psychiatrists in March and May 1989. Because the response rate of the residency directors was above 60% from one mailing (June 1989), a second mailing was not sent.

The question about the timing of *DSM-IV*'s publication was worded as follows: "*DSM-IV* is scheduled for publication in 1992. Do you believe that the proposed five-year interval between the publication of *DSM-III-R* and *DSM-IV* is: just right, too long, or too short?" At the time the questionnaire was developed, published reports indicated that *DSM-IV* was scheduled for release in 1992, although at the time of this writing the scheduled publication date has been pushed back to 1993 (1). The respondents were also asked to recommend the year in which *DSM-IV* should be published and to recommend a general guideline for the number of years separating *DSM* editions. For those subjects who denoted a range of years we used the midpoint value (rounded off to the nearest even-numbered integer if the midpoint was a fraction).

Categorical variables were compared by chi-square analysis without Yates' correction or Fisher's exact test if the expected value in any cell of a 2×2 table was less than 5. We used t tests or one-way analyses of variance in comparing continuous variables.

RESULTS

Of the 1,000 questionnaires mailed to the random sample of practicing American psychiatrists, 48 could

TABLE 2. Opinions of Psychiatrists About the Proposed 5-Year Interval Between Publication of *DSM-III-R* and *DSM-IV*

Opinion	A: Practicing Psychiatrists (N=454)		B: Researchers (N=196)		C: Residency Directors (N=128)		D: Residents (N=1,331)		χ^2 (df=3)	p	Significant Two-Group Differences
	N	%	N	%	N	%	N	%			
Just right	155	38.6	54	29.7	50	40.3	553	44.7	17.05	0.001	D>A[a], D>B[b], A>B[a]
Too long	15	3.7	6	3.3	2	1.6	46	3.7	1.53	n.s.	
Too short	232	57.7	122	67.0	72	58.1	639	51.6	17.96	0.001	B>A[a], B>D[b], A>D[a]
Data missing	52	—	14	—	4	—	93	—	—	—	

[a] $p<0.05$.
[b] $p<0.001$.

not be delivered. The response rate of the 952 subjects who received the questionnaire was 47.7% (N=454). The response rate for the 337 researchers was 58.2% (N=196), and it was 64.6% (N=128) for the 198 residency directors. By survey research standards, these are high response rates for a three–four-page questionnaire from a nonauthoritative source (5).

The practicing psychiatrists were representative of domestic APA membership in terms of country of undergraduate medical education and age, but the group was not representative in that it contained proportionately more men and more who practiced in the western United States (D. Schumaier, APA Office of Membership, personal communication). Demographic and background characteristics of the random sample, researchers, and residents are detailed in table 1. The mean±SD ages for the three groups were 50.1±11.7, 43.7±8.7, and 33.2±5.3 years, respectively. The random sample of practitioners had 17.1±11.0 years of experience and the researchers, 13.3±9.0 years. Although we intended that the survey be distributed only to residents in their third or fourth postgraduate year (PGY-3 or PGY-4), we received responses from 13 residents in PGY-1, 94 in PGY-2, and 14 in PGY-5 and from 14 fellows. For the residents in PGY-3 and PGY-4 the response rate was 48.4% (N=1,196). There was no difference among the five resident groups in attitude about the *DSM-IV* publication date (χ^2= 2.65, df=4, n.s.); therefore, we combined the resident groups for analysis.

The majority of all four groups believed that *DSM-IV* is being published prematurely, and this opinion was strongest among the researchers (table 2). The 1,065 respondents who endorsed this view were asked in what year *DSM-IV* should be published. Fifty-one subjects did not respond to this question, 16 wrote that it should never be published, 34 indicated that publication should occur when the data warrant it, and 21 noted that it should be published whenever needed. The median recommended year of publication was similar in the four groups, ranging from 1995 to 1997.

All respondents were asked to recommend a general guideline for the interval between *DSM* editions. Seventy-nine subjects did not answer this question. Eight subjects said never, 24 indicated that publication should occur when the data warrant it, 15 recommended that editions be published as needed, 14 did not know, and 15 wrote other suggestions. The median interval recommended was 8 years by the residents and 10 years by the three other groups. One-sixth of the nonresident subjects recommended that *DSM* editions be separated by more than 10 years, and one-half recommended an 8–10-year interval.

We examined correlates of respondents' opinions about a 5-year interval between *DSM-III-R* and *DSM-IV* (table 3). Within each group no association was found between the opinion about the interval and the respondents' Board certification status, ownership of *DSM-III* or *DSM-III-R*, length of time the physician had used *DSM-III*, and whether the physician was currently using *DSM-III* or *DSM-III-R* as his or her primary diagnostic reference. Compared to individuals who believed that the 5-year interval was just right, those who believed that the interval was too short had more years of professional experience. Among practicing psychiatrists, those who felt the interval was just right had 14.9±10.2 years of experience, and those who felt the interval was too short had 17.5±11.0 years of experience (t=2.34, df=380, $p<0.05$). Among the researchers, the figures were 11.9±6.8 and 13.5±9.8 years, respectively (t=1.28, df=143, n.s.). All four groups were consistent in their opinion about the interval between *DSM* editions; those who believed that the *DSM-III-R*/*DSM-IV* interval was too short also believed that this was true of the *DSM-III*/*DSM-III-R* interval. In addition, in all four groups, those who believed that the *DSM-III-R*/*DSM-IV* interval was too short were less likely to believe that *DSM-III-R* was needed.

Finally, we examined who the respondents thought should determine the need for, and nature of, future editions of *DSM*. The researchers, residency directors, and residents wanted a consensus of researchers to be the deciding body. The practitioners, however, were about equally divided between researcher consensus and the majority of the APA membership. Moreover, practitioners who believed that the *DSM-III-R*/*DSM-IV* interval was just right more frequently wanted the researchers to control the *DSM* process, whereas individuals who believed that the interval was too brief preferred to have the APA membership make the decision about *DSM* revisions (table 3).

TABLE 3. Correlates of Psychiatrists' Opinions About the Proposed 5-Year Interval Between the Publication of *DSM-III-R* and *DSM-IV*

	Practicing Psychiatrists[a]				Researchers[b]				Residency Directors[c]				Residents[d]			
	Just Right (N=155)		Too Short (N=232)		Just Right (N=54)		Too Short (N=122)		Just Right (N=50)		Too Short (N=72)		Just Right (N=553)		Too Short (N=639)	
Item	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Philosophy of practice																
Psychodynamic	34	22.2	67	29.0	4	7.4	13	10.7					142	25.8	156	24.6
Biological	54	35.3	83	35.9	27	50.0	65	53.7					183	33.2	227	35.8
Eclectic	61	39.9	69[e]	29.9	19	35.2	36	29.8					211	38.3	238	37.5
Other	4	2.6	12	5.2	4	7.4	7	5.8					15	2.7	13	2.1
Primary professional activities																
Administration	28	18.2	27	11.7	20	37.0	43	35.8					43	7.8	46	7.2
Teaching	25	16.2	41	17.7	28	40.7	55	45.8					136	24.7	129	20.2
Private practice	99	64.3	144	62.3	11	20.4	22	18.3					268	48.6	337	52.7
Research	7	4.5	25[e]	10.8	40	74.1	75	62.5					58	10.5	77	12.1
Salaried clinical practice	56	36.4	90	39.0	12	22.2	16	13.3					250	45.4	269	42.1
Opinion about the *DSM-III*/*DSM-III-R* interval																
Just right	113	75.8	63[f]	27.9	36	69.2	35[f]	29.9	38	80.9	30[f]	43.5	324	65.2	220[f]	37.0
Too long	26	17.4	6[f]	2.7	10	19.2	0[f]	0.0	5	10.6	2	2.9	143	28.8	9[f]	1.5
Too short	10	6.7	157[f]	69.5	6	11.5	82[f]	70.1	4	8.5	37[f]	53.6	30	6.0	365[f]	61.4
Was *DSM-III-R* needed?																
No	22	14.2	124[f]	53.4	4	7.4	58[f]	47.9	7	14.3	21	29.2	35	6.3	204[f]	31.9
Yes	99	63.9	51[f]	22.0	33	61.1	34[f]	28.1	32	65.3	23[f]	31.9	377	68.3	180[f]	28.2
Not sure	34	21.9	57	24.6	17	31.5	29	24.0	10	20.4	28[e]	38.9	140	25.4	255[f]	39.9
Major reasons for publishing *DSM-III-R*																
Correction of problems	103	67.8	122[g]	54.5	42	80.8	76[e]	63.3	28	57.1	41	59.4	381	70.0	360[f]	58.8
New research warranted it	101	66.4	89[f]	39.7	33	63.5	45[g]	37.5	40	81.6	35[f]	50.7	382	70.2	320[f]	52.3
Financial benefit to APA	12	7.9	66[f]	29.5	7	13.5	46[g]	38.3	6	12.2	16	23.2	31	5.7	121[f]	19.8
Politics	10	6.6	20	8.9	1	1.9	6	5.0	2	4.1	2	2.9	15	2.8	44[f]	7.2
Personal benefit to individual involved	0	0.0	13[g]	5.8	1	1.9	8	6.7	0	0.0	0	0.0	3	0.6	10	1.6
Do not know of any reasons	2	1.3	8	3.6	0	0.0	2	1.7	2	4.1	2	2.9	7	1.3	20[e]	3.3
Who should determine need for future *DSMs*?[h]																
Majority of APA membership	58	38.2	102	44.9	8	15.1	20	16.7	13	26.0	13	18.9	185	34.2	112[e]	17.9
APA leadership	30	19.7	39	17.2	6	11.3	23	19.2	15	30.0	17	24.6	100	18.5	112	17.9
Consensus of researchers	82	53.9	96[e]	42.3	39	73.6	82	68.3	35	70.0	46	66.7	309	57.1	315[e]	50.3

[a] Data missing for philosophy of practice (N=2), primary professional activities (N=3), opinion about *DSM-III*/*DSM-III-R* interval (N=5), major reasons for publishing *DSM-III-R* (N=11), and who should determine future *DSMs* (N=8). Six individuals used criteria other than *DSM-III* or *DSM-III-R*, and seven had no opinion or were not sure about the length of the *DSM-III*/*DSM-III-R* interval.

[b] Data missing for philosophy of practice (N=1), primary professional activities (N=2), opinion about the *DSM-III*/*DSM-III-R* interval (N=3), need for *DSM-III-R* (N=1), major reasons for publishing *DSM-III-R* (N=4), and who should determine future *DSMs* (N=3). Two individuals used criteria other than *DSM-III* or *DSM-III-R* and four had no opinion or were not sure about the length of the *DSM-III*/*DSM-III-R* interval.

[c] Residency directors' survey did not include the questions for years of professional experience. Data missing for opinion about *DSM-III*/*DSM-III-R* interval (N=4), need for *DSM-III-R* (N=1), and who should determine future *DSMs* (N=3). Two individuals had no opinion or were not sure about the length of the *DSM-III*/*DSM-III-R* interval.

[d] Data missing for philosophy of practice (N=7), primary professional activities (N=2), opinion about the *DSM-III*/*DSM-III-R* interval (N=46), need for *DSM-III-R* (N=1), reasons for publishing *DSM-III-R* (N=36), and who should determine future *DSMs* (N=25). Four individuals used criteria other than *DSM-III* or *DSM-III-R*, and 55 had no opinion or were not sure about the length of the *DSM-III*/*DSM-III-R* interval.

[e] $p<0.05$ (chi-square analysis).

[f] $p<0.001$ (chi-square analysis).

[g] $p<0.01$ (chi-square analysis).

[h] Percentages add to more than 100 because respondents checked more than one choice, despite instructions to check only one.

DISCUSSION

We surveyed four groups of psychiatrists and found that the majority of each group believed that *DSM-IV* is being published prematurely. A limitation of this survey is that the question about the *DSM-III-R*/*DSM-IV* interval asked about a 5-year interval between editions rather than a 6-year interval. However, in this context it is important to note that only five of the 925 individuals who indicated that the interval was too short recommended 1993 as the *DSM-IV* publication date.

If there is a silver lining in these findings, it is the trend that the residents and more recently trained practicing psychiatrists were less likely to believe that *DSM-IV*'s publication will be premature. Perhaps the new generation of psychiatrists feel more comfortable adapting to changes in diagnostic criteria, or perhaps they lack the experience to appreciate the difficulties encountered when criteria change.

The belief that *DSM-IV* is being published too soon could contribute to underutilization of *DSM-IV* by substantial numbers of psychiatrists. Supporting this contention is the fact that compared to practicing psychiatrists who thought that the *DSM-III/DSM-III-R* interval was appropriate, those who believed that *DSM-III-R* was published too soon were more likely to still be using *DSM-III* (36.0% [N=63] versus 25.3% [N=57]; $\chi^2=5.33$, df=1, $p<0.05$). Thus, because *DSM-IV* will inevitably appear in 1993, to foster compliance with it, APA must persevere in its efforts to demonstrate that the advantages of publishing it in 1993 outweigh the disadvantages of accepting yet another manual.

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Neuropsychological Performance in Medicated and Unmedicated Patients With Tourette's Disorder

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Objective: To date, there have been no formal investigations of neuropsychological performance in patients with Tourette's disorder who are taking psychotropic medications. The authors conducted this study to provide such information. Method: They examined the neuropsychological performance of 96 patients 6–18 years old who met DSM-III-R *criteria for Tourette's disorder; 51 of these patients were taking neuroleptic medications and 45 were not. The groups were well matched with regard to age, sex, education, and duration of symptoms. Each group was given a complete neuropsychological test battery as well as instruments rating symptoms of Tourette's disorder, obsessive-compulsive characteristics, and other behavioral disturbances. Results: The patients taking medications did not differ from those not taking medications on any of the neuropsychological, intellectual, or educational measures. In addition, the groups did not differ with regard to level of Tourette's disorder symptoms. Conclusions: The results of this investigation suggest that patients with Tourette's disorder who do not experience intolerable side effects from neuroleptic medications are able to perform on educational, intellectual, and neuropsychological tests at a level comparable to that of unmedicated patients. These results have positive implications for patients with Tourette's disorder who respond to neuroleptic medications.*

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Tourette's disorder is a complex neuropsychiatric syndrome characterized by simple and complex motor and phonic tics. Numerous somatic and nonsomatic treatments have been used, but there is increasingly general acceptance of a neurochemical abnormality as the pathophysiological substrate of Tourette's disorder (1). The focus on neurochemical mechanisms arises to some extent from the utility of various neuroleptic drugs in the treatment of this disorder. Several studies have demonstrated the effectiveness of haloperidol at doses much lower than those used in the treatment of major psychiatric disorders (2). Haloperidol has been the most widely used medication in the treatment of Tourette's disorder, but more recently other drugs (e.g., pimozide and clonidine) have been proposed as useful treatments for the symptoms of Tourette's disorder (3, 4).

Although the doses of neuroleptics used are typically low, the possibility of adverse side effects, including cognitive impairment, is problematic, particularly for children of school age. Cognitive impairments such as sedation, declining school performance, and decreased motivation may occur at doses varying from 2 to 10 mg/day (2). A recent survey of a large group of patients with Tourette's disorder (5) revealed that approximately 70% of the patients reported having taken medications for their symptoms at some time, although only 43% were taking medications at the time of the survey. Many of the patients in that survey indicated that although the medications were effective in controlling Tourette's disorder symptoms, the side effects were intolerable.

To date, there have been no formal investigations of neuropsychological performance in patients with Tourette's disorder who were taking psychotropic medications. The current study was performed to address this question. We compared Tourette's disorder patients who were taking neuroleptic medications with Tourette's disorder patients who were not taking medications. It should be emphasized from the outset that the inferences about medication effects generated are necessarily limited. The most direct examination of medication effects is to study the same group of patients before and after initiation of treatment, but in many studies of clinical groups, including the current one, this is not possible. The present investigation is strictly limited to a comparison of patients with

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Tourette's disorder who were or were not taking neuroleptic medications.

METHOD

The study group consisted of 96 patients between the ages of 6 and 18 years who met *DSM-III-R* criteria for Tourette's disorder. All patients had the diagnosis of Tourette's disorder confirmed by a neurologist or psychiatrist. The mean±SD age of this group was 12.25±2.96 years. Eighty-four of the patients were right-handed, and 12 were left-handed. All of the patients were volunteers who were recruited specifically for participation in this study. Patients were contacted and advised of the nature of this study through the Tourette Syndrome Association of Ohio, which maintains a computerized patient registry. Parents of all patients were informed of the nature and purpose of this study, and informed consent was obtained for each patient. Patients were provided a small financial compensation for their participation.

The patients were divided into two groups: those who were taking medications for their Tourette's disorder symptoms (N=51) and those who were not (N=45). Of the latter group, 22 had taken medications in the past, but not within the previous 3 months, and 23 had never taken medications for their symptoms. Among the medicated patients, the most frequently taken drugs were clonidine (N=21), pimozide (N=15), and haloperidol (N=13). Most patients were taking only one medication, but 11 were taking more than one. All of the patients were taking very low doses of the neuroleptic medications in the ranges typically used in the treatment of patients with Tourette's disorder. The characteristics of the medicated and unmedicated groups are presented in table 1, which reveals that the groups were similar in age, education, IQ, and duration of symptoms. There were 43 boys and eight girls in the medicated group and 39 boys and six girls in the unmedicated group (χ^2=0.01, df=1, n.s.).

The neuropsychological test battery included the Wechsler Intelligence Scale for Children—Revised (WISC-R) for patients between the ages of 6 and 15 and the Wechsler Adult Intelligence Scale—Revised (WAIS-R) for those older than 15. In addition, the test battery included the Wide Range Achievement Test (6), the Wisconsin Card Sorting Test (7), the Grooved Pegboard Test (8), and an expanded Halstead-Reitan battery (9). The Halstead-Reitan battery included the Category Test, the Tactual Performance Test—Time, the Tactual Performance Test—Memory, the Tactual Performance Test—Location, the Speech Sounds Perception Test, the Seashore Rhythm Test, the Trail Making Test (parts A and B), the Finger Tapping Test, and measures of finger agnosia and graphesthesia. All motor and sensory tasks were performed with both dominant and nondominant hands.

TABLE 1. Characteristics and Neuropsychological Test Scores of Medicated and Unmedicated Patients With Tourette's Disorder

	Medicated Patients (N=51)		Unmedicated Patients (N=45)		
Item	Mean	SD	Mean	SD	t (df=94)
Characteristics					
Age (years)	11.8	2.9	12.8	3.0	1.66
Education (years)	5.8	2.8	6.6	2.9	1.39
Verbal IQ	100.3	15.4	103.1	16.2	0.86
Performance IQ	98.9	16.0	102.7	12.8	0.20
Duration of symptoms (months)	6.1	3.6	7.0	3.1	0.21
Neuropsychological test scores					
Category Test	42.5	14.4	41.4	13.7	0.39
Tactual Performance Test					
Time	36.7	26.4	33.1	27.9	0.64
Memory	53.9	15.3	57.8	15.4	1.26
Location	48.4	14.4	49.1	12.5	0.27
Seashore Rhythm Test	53.3	10.5	53.6	12.4	0.12
Speech Sounds Performance Test	43.1	16.4	48.0	13.4	1.46
Trail Making A	52.9	19.4	42.6	27.4	2.09[a]
Trail Making B	47.7	25.8	43.6	18.7	0.84
Wide Range Achievement Test					
Reading	97.7	16.4	99.1	16.5	0.42
Spelling	97.7	16.4	98.7	19.2	0.43
Arithmetic	91.7	15.9	96.5	22.7	1.16
Wisconsin Card Sorting Test					
Categories	42.8	13.3	43.5	12.8	0.25
Perseveration	50.8	9.7	49.6	14.1	0.45
Logical memory[b]	80.2	21.1	84.6	17.9	1.11
Visual reproduction[b]	79.2	21.3	79.9	19.8	0.19
Finger Tapping Test					
Dominent hand	42.6	9.9	47.2	9.7	2.30[a]
Nondominant hand	47.6	11.2	50.4	10.4	1.27
Grooved Pegboard Test					
Dominant hand	42.2	22.9	42.8	20.4	0.15
Nondominant hand	31.9	24.8	37.9	27.1	1.12
Finger agnosia					
Dominant hand	24.2	47.9	30.5	44.5	0.67
Nondominant hand	34.8	37.9	39.4	31.8	0.65
Graphesthesia					
Dominant hand	29.1	57.9	22.5	46.6	0.62
Nondominant hand	31.6	56.8	23.1	44.4	0.83

[a] $p<0.05$, uncorrected. After Bonferroni correction for multiple analyses the difference was not significant.

[b] From the Wechsler Memory Scale, Revised: proportional recall=(delayed recall/immediate recall)×100.

The scores from the Wechsler intelligence scales and the Wide Range Achievement Test are derived on an age-corrected basis and, therefore, are comparable across age levels. However, because the scores from the neuropsychological test battery are not derived on an age-corrected basis, it was necessary to convert the raw scores to age-corrected scores to permit comparisons of performance. The raw scores from the Halstead-Reitan battery and from associated measures were converted to age-corrected t scores according to published normative data on these tests (10–12).

The t scores were computed with a mean of 50 and a standard deviation of 10 in reference to appropriate age norms.

In addition to the neuropsychological measures, a rating of Tourette's disorder symptoms was obtained by using the Tourette Syndrome Symptom List (13). This measure elicits ratings (by patients and/or parents) of the frequency or severity of a broad range of simple and complex symptoms. For each of 20 symptoms, ratings were obtained on a scale ranging from 0 (symptom free) to 5 (almost always). Each patient was rated on the Tourette Syndrome Symptom List for the week preceding the neuropsychological evaluation. The data from the Tourette Syndrome Symptom List were analyzed to provide measures of the number of symptoms reported, the prominence of each symptom in the week preceding the examination, and the severity of simple and complex symptoms in the week preceding the examination.

In addition to the Tourette Syndrome Symptom List, parents of patients were asked to complete the Child Behavior Checklist (14) and the Connors Parent Rating Scale (15). A rating of obsessive-compulsive symptoms (16) was also obtained.

RESULTS

The initial data analysis consisted of a comparison of the neuropsychological t scores of the medicated and unmedicated groups. Because the groups were well matched with respect to age, sex, and education, it was not necessary to control statistically for the effects of these measures on neuropsychological performance. Data were analyzed by using t tests for independent groups. The results of these analyses are presented in table 1, which reveals that there were no significant differences on any of the neuropsychological measures. The two groups also did not differ in the proportion of patients obtaining scores below normative levels.

The behavioral rating scale scores of the two groups of patients were also compared. There were no differences between groups on ratings of simple tics, complex tics, obsessive-compulsive symptoms, or any of the subscales from the Connors Parent Rating Scale. Analysis of the Child Behavior Checklist was complicated by the fact that the test generates different scales for the various age and sex subgroups. There were too few girls in the study group to permit statistical comparisons by sex. There were no differences on any of the Child Behavior Checklist subscales among the boys 12 years old and older. However, among the younger subgroup, medicated patients were rated as being more anxious ($t=2.84$, $df=28$, $p<0.01$), depressed ($t=3.59$, $df=28$, $p<0.01$), and aggressive ($t=2.84$, $df=28$, $p<0.01$) and as having more obsessive-compulsive symptoms ($t=3.42$, $df=28$, $p<0.01$) than unmedicated patients.

DISCUSSION

These data represent the first direct comparisons of neuropsychological performance in medicated versus unmedicated patients with Tourette's disorder. The medicated and unmedicated groups were very similar in regard to age, sex, education, and duration of Tourette's disorder symptoms. There are a number of important methodological considerations that would appear to represent clear advantages of the current investigation. This study was based on a large group of children meeting diagnostic criteria for Tourette's disorder (N=96) and was not based on patients who had been referred to a clinic. All subjects were recruited specifically for the purposes of participation in this research project, which would reduce bias related to clinical ascertainment. It could be argued, however, that patients (or their parents) who volunteer for such studies may not be representative of the patient population as a whole. Although this may be the case, the IQ distribution of the medicated and unmedicated groups suggests that the abilities of these two groups of patients very closely approximate the normal distribution. This would appear to support the suggestion that this group of patients is representative of the larger population of patients with Tourette's disorder.

In addition to normal IQ levels, patients in both groups had normal scores for their ages on the Wide Range Achievement Test, which suggests normal educational attainment. We found no differences between medicated and unmedicated groups on the neuropsychological measures. The lack of differences in IQ, educational, and neuropsychological measures seems to suggest that at the doses used there were no substantial adverse effects of neuroleptic medications on the patients' neuropsychological performance. Although these results suggest no significant effects on performance, some issues merit consideration.

The patients taking medications whom we studied may be a biased group to some extent: these patients might have continued to take the medications because of a relative lack of adverse side effects, but patients who did experience side effects might have discontinued them. The incidence and severity of cognitive side effects among our medicated patients, therefore, may have been underrepresented. It is clear that the most direct approach to documentation of adverse cognitive effects of these medications is to examine the same patients before and after drug administration. However, the current data suggest that those patients who do not experience intolerable side effects are capable of normal educational attainment and performance on neuropsychological tasks.

It could be argued that although the medications may produce slight side effects, the beneficial effects in terms of symptom control outweigh these negative effects. Virtually all of the patients who were taking medications reported that their level of symptoms was better while they were taking medications than it was while they were not taking medications. The groups did not differ in terms of symptoms of Tourette's disorder or obsessive-compulsive disorder, but the younger patients who were receiving medications were rated by their parents as having more emotional adjustment problems on the Child Behavior Checklist. It may be that patients with more severe symptoms are more likely to take medications than are patients with less severe symptoms. The finding that some of the medicated patients with Tourette's disorder had more emotional adjustment problems in spite of having no differences in their level of Tourette's disorder symptoms may reflect the specific beneficial effect of medications on the symptoms of Tourette's disorder rather than on associated behavioral disturbances.

It could also be argued that although the groups were matched in age, sex, and education, they differed in other important characteristics, such as the severity of their Tourette's disorder. The unmedicated group was composed of 23 patients who had never been given medication as well as 22 who had taken neuroleptic medications in the past. It is possible that there were some differences between these two subgroups and that combining them may have concealed differences between the unmedicated group and the medicated group. We explored this possibility by comparing the two subgroups of unmedicated patients on the neuropsychological and symptom variables. There were no differences between the patients who had never taken medication and those who had taken neuroleptic medications in the past on any of the measures supporting the idea that the unmedicated patients may have had less severe symptoms. The fact that the medicated patients performed at a level comparable to that of the unmedicated patients suggests that the medications may result in enough control of symptoms to permit these patients to perform at a level comparable to that of unmedicated patients.

The results of this investigation suggest that patients with Tourette's disorder who do not experience intolerable side effects from neuroleptic medications are able to perform on educational, intellectual, and neuropsychological tests at a level comparable to that of unmedicated patients. It is likely that these findings are applicable only to those patients who are able to continue to take medications without side effects. Although the possibility of mild side effects in the medicated patients in this study cannot be eliminated, the findings suggest that the beneficial effects in terms of symptom control outweigh these side effects. These results have positive implications for patients who respond to neuroleptic medications. They suggest that concerns regarding adverse effects on school performance may be reduced for these patients. Obviously, use of these medications in any patient, especially a child, requires constant clinical monitoring and dose titration to achieve the maximal therapeutic benefit with minimal side effects. The present data suggest that in cases where this is accomplished, substantial adverse effects on cognitive and intellectual performance can be avoided.

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Relations Among Clinical Scales in Schizophrenia

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Objective: Clinical scales have become established as tools to quantify phenomenological features of schizophrenia. The goal of this study was to examine relations among the following: the Brief Psychiatric Rating Scale (BPRS), the Scale for the Assessment of Positive Symptoms, the Scale for the Assessment of Negative Symptoms, and the deficit-nondeficit classification. Method: Forty-seven patients with schizophrenia were recruited according to specific inclusion and exclusion criteria. The standardized assessment procedures were administered by a trained psychiatric research team. Results: Examination of the BPRS showed that the patients had highest scores on the thought disorder factor and the symptoms specific to schizophrenia. Classification of patients as having the positive, negative, or mixed type of schizophrenia resulted in a finding of seven with the positive, seven with the negative, and 33 with the mixed type. The division of patients into those with the deficit syndrome (N=29) and those without (N=18) was related to symptom specificity and to positive and negative symptoms. Deficit syndrome patients had more symptoms specific to schizophrenia, fewer nonspecific symptoms, and, as expected, greater severity of negative symptoms. Cluster analysis revealed three clusters of patients: those with low negative symptom scores and high scores on specific symptoms (the majority were without the deficit syndrome); those with high scores on negative, positive, and specific symptoms (the majority had the deficit syndrome); and those with lower scores on specific symptoms and high scores on negative and positive symptoms (the majority had the deficit syndrome). Conclusions: The scales showed some overlap but also seemed to measure complementary aspects of the phenomenology of schizophrenia. Subtypes of patients identified by the combined use of these scales may differ in underlying pathology.

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A challenge for schizophrenia research is dealing with the heterogeneity of the disorder. It has been recognized that schizophrenia may not have a uniform presentation and course. Even among patients who meet rigorous diagnostic criteria, there appear to be several clinical subtypes (*DSM-III-R*). Although variability in symptoms and course occurs in any disease, such variability may point to different underlying pathophysiology of subtypes. Several clinical rating scales and classification methods have been used for schizophrenic patients, and it is important to compare them in a single sample to determine their overlap and differences. The goals of this study were to compare the scales and examine symptom clusters. This may help identify subpopulations with specific etiologies or treatment responses.

The widely applied Brief Psychiatric Rating Scale (BPRS) (1) covers a broad range of symptoms and does not sample schizophrenic symptoms in detail. One subdivision of items is based on factor analysis, which has indicated five factors: anxiety-depression, anergia, thought disorder, activity, and hostility (2). Gur et al. (3) used another subdivision, dividing BPRS items into symptoms considered specific to schizophrenia and those that are not a hallmark of schizophrenia. They reported higher scores on the specific symptoms for schizophrenic patients than for depressed patients and correlations between severity of specific symptoms and

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neurophysiologic patterns measured by regional cerebral blood flow and glucose metabolism.

Andreasen emphasized the importance of negative and positive symptoms and developed the Scale for the Assessment of Negative Symptoms (4, 5) and the Scale for the Assessment of Positive Symptoms (6). Andreasen and Olsen (7) reported that about one-third of patients with schizophrenia were characterized by positive symptoms, one-third had predominantly negative symptoms, and one-third had mixed symptoms. This classification is based on cross-sectional data. Carpenter et al. (8) proposed that deficit symptoms, the primary enduring negative symptoms of schizophrenia, should be distinguished from transient negative symptoms secondary to other factors. The criteria for schizophrenia with deficit syndrome are based on a longitudinal evaluation over the preceding 12 months.

This study examined relationships among the BPRS, the scales for positive and negative symptoms, and the deficit-nondeficit classification. Such research is essential for the evolution of comparable characterization of patients across research centers and will provide information on the degree of overlap among subscores on each scale and among the scales. These comparisons were used to test the hypotheses 1) that the majority of schizophrenic patients can be classified as having primarily the positive or the negative type of the disorder and that this relates to the deficit-nondeficit typology and 2) that there is a higher correlation between the severity of symptoms depicted by the positive and negative symptom scales and the schizophrenia-specific items of the BPRS than the nonspecific items of the BPRS.

METHOD

Patients were recruited through our Mental Health Clinical Research Center inpatient and outpatient programs. Members of the assessment team reviewed data on each potential participant and assessed suitability. They excluded patients 1) who had histories of any other *DSM-III-R* axis I disorders, 2) who had histories of substance abuse according to *DSM-III-R* criteria and toxic screen, 3) who had previously received ECT or depot medication, 4) who had histories of any neurological or medical disorders, and 5) whose native language was not English.

Suitability for the study was determined in two phases. First, a structured screening that included information from referring family members, mental health professionals, and review of records was conducted. Of 147 consecutive potential patients who underwent this structured screening, 61 were acceptable, and they underwent a comprehensive evaluation. This included detailed history; physical, neurological, and psychiatric examinations; and laboratory studies. The Structured Clinical Interview for DSM-III-R (9) was administered, and the assessment team made a best-estimate consensus diagnosis. In addition to the completed standard forms, a narrative summarized each patient's history and clinical presentation. Of the 61 patients who received the comprehensive evaluation, 47 were admitted to the study and were studied while they were not taking medication, as part of the research center protocols. Patients were excluded in the screening and comprehensive assessment for the following reasons: medical illness (N=13), another axis I diagnosis (N=23), ECT (N=11), substance abuse (N=24), depot medication (N=6), head trauma (N=7), other neurological history (N=11), declined, unavailable, or unable to comprehend the meaning of consent (N=19) (some patients were excluded for more than one reason). Informed consent was obtained after the procedures had been fully explained.

Scales and Scoring

The following scales were completed: the BPRS, the Scale for the Assessment of Negative Symptoms, the Scale for the Assessment of Positive Symptoms, and an assessment according to the deficit-nondeficit typology. Other scales were also completed but will not be analyzed here. The BPRS and the negative and positive symptom scales were completed for each patient by two members from among the assessment team (R.E.G., P.D.M., S.M.R., S.L.), who had been trained to a criterion reliability of 0.90 (intraclass correlation). The ratings were reviewed by the entire assessment team, and disagreements were resolved by consensus; the consensus ratings were used in the study.

The BPRS was completed on the basis of the clinical interviews and observations. It was scored in two ways: 1) the average ratings for the five factors of anxiety-depression, anergia, thought disorder, activity, and hostility and 2) scores when the items were divided into a subgroup of symptoms relatively specific to schizophrenia (emotional withdrawal, conceptual disorganization, mannerism and posturing, grandiosity, suspiciousness, hallucinatory behavior, unusual thought content, blunted affect) and a subgroup of relatively nonspecific symptoms (somatic concerns, anxiety, guilt feelings, tension, depressive mood, hostility, motor retardation, uncooperativeness, excitement, disorientation) (3).

The Scale for the Assessment of Negative Symptoms and the Scale for the Assessment of Positive Symptoms were completed on the basis of the comprehensive evaluation, the structured clinical interview, review of records, and interviews with family members. The evaluation was based on data from the month preceding the patient's admission to the protocol. Scoring was done according to Andreasen and Olsen's (7) division into five negative symptom scores and four positive symptom scores and as average negative and positive symptom scores. Two measures are obtained for each negative and positive symptom complex: a global rating and average ratings of items included in each symptom complex. The former requires rating of the impact of the symptoms on the patient's ability to

TABLE 1. Rotated Factor Loadings of Scores of 47 Schizophrenic Patients on the Subscales of the Scale for the Assessment of Negative Symptoms and the Scale for the Assessment of Positive Symptoms

Subscale	Factor 1	Factor 2	Factor 3
Negative symptom scale			
Affective flattening	0.86[a]	0.10	−0.10
Alogia	0.83[a]	0.34	−0.17
Avolition-apathy	0.81[a]	−0.08	0.13
Anhedonia-asociality	0.80[a]	−0.01	0.24
Attention	0.54	0.69[a]	−0.12
Positive symptom scale			
Hallucinations	0.20	0.21	0.78[a]
Delusions	−0.08	0.05	0.90[a]
Bizarre behavior	0.14	0.88[a]	0.14
Positive thought disorder	−0.28	0.73[a]	0.39
Percent of total variance	35	22	19

[a]Highest loading across factors.

TABLE 2. Intercorrelations Among Summary Scores of 47 Schizophrenic Patients on the Scale for the Assessment of Negative Symptoms, the Scale for the Assessment of Positive Symptoms, and the BPRS

Measure	1	2	3	4	5	6
Negative symptom scale						
1. Average of scores		0.95[a]	0.11	0.19	0.43[b]	0.12
2. Global score			0.04	0.14	0.38[b]	0.08
Positive symptom scale						
3. Average of scores				0.87[a]	0.56[a]	0.47[a]
4. Global score					0.61[a]	0.36[c]
BPRS						
5. Schizophrenia-specific items						0.44[b]
6. Nonspecific items						

[a]$p<0.001$.
[b]$p<0.01$.
[c]$p<0.05$.

function. The main analyses were performed, as recommended, on the global ratings for each symptom complex, but they were also repeated for the averages, with similar results.

To assess the subjects according to the deficit-nondeficit concept of Carpenter et al. (8), the assessment team reviewed information regarding the patient's clinical status during the preceding 12 months, and a consensus was achieved. This information was obtained from our follow-up evaluations, interviews with family members, review of records, and continual contact with psychiatrists and other mental health professionals who treated the patient. Not all patients were followed up for a whole year by a research psychiatrist from our center, but for every patient we obtained from multiple sources comprehensive data that were consistent with our assessment and in which we have confidence. An independent evaluation by one investigator resulted in one instance of disagreement that was resolved after discussion. Patients who did not meet the criteria for the deficit syndrome were classified as having the nondeficit type of schizophrenia.

Data Analysis

Each scale was first evaluated by obtaining scatterplots and calculating the product-moment correlations among subscores. Hypothesis 1 was tested by applying Andreasen's criteria to the global ratings on the negative and positive symptom scales and comparing the distribution to that expected from Andreasen's model (one-third of the ratings indicating the positive, one-third the negative, and one-third the mixed type of schizophrenia). Hypothesis 2 was tested by correlating the severity of symptoms across the negative and positive symptom scales with the BPRS subscores for items specific and nonspecific to schizophrenia. The scores were z-transformed (mean±SD=0±1) for this purpose.

To evaluate the factorial structure of the negative and positive symptom scales, a principal components analysis was applied to the correlations between all pairs of symptom scores. The differences between patients with deficit and nondeficit schizophrenia on the dependent measures derived from the BPRS and the negative and positive symptom scales were tested by multivariate analysis of variance (SAS GLM procedure) (10). Deficit-nondeficit was a grouping factor, and summary negative and positive scale scores and subscores (i.e., the five negative symptom and four positive symptom subscores) were the within-group (repeated measures) factors. To evaluate formally the existence of subtypes, we used Ward's method (11) to do a cluster analysis, and made scatterplots of the summary scale scores. Clusters were examined for frequency of deficit and nondeficit subtypes by using the chi-square statistic (corrected for attenuation when appropriate) as well as the Cochran-Mantel-Haenszel statistic for general association (12, 13) to test association across clusters. Because of the sample size, we limited the number of clusters to three.

RESULTS

Individual Scales

The subjects had a mean±SD score of 57.70±11.68 on the BPRS (range=37–84). As expected in a sample of schizophrenic patients, they scored higher on the symptoms specific to schizophrenia than on the nonspecific ones ($t=5.14$, $df=45$, $p<0.0001$). Indeed, all but two patients had higher severity ratings for the specific symptoms of schizophrenia.

The correlations between scores on the BPRS specific symptoms and the five BPRS factors were significant for anergia ($r=0.55$), thought disorder ($r=0.88$), and activity ($r=0.49$) ($df=46$, each $p<0.0001$) and nonsignificant for anxiety-depression and hostility ($r=0.25$ and $r=0.18$, respectively). By contrast, nonspecific symptom scores were correlated highly with scores on anxiety-depression ($r=0.70$), activity ($r=0.63$) (each $p<0.0001$), and hostility ($r=0.42$, $p<$

TABLE 3. Pearson Correlation Coefficients for BPRS Factor Scores and Subscale Scores of 47 Schizophrenic Patients on the Scale for the Assessment of Negative Symptoms and the Scale for the Assessment of Positive Symptoms

	BPRS Factor				
Subscale	Anxiety-Depression	Anergia	Thought Disorder	Activity	Hostility
Negative symptom scale					
Affective flattening	−0.26	0.66[a]	0.08	−0.13	0.19
Alogia	−0.33[b]	0.69[a]	0.02	0.00	0.16
Avolition-apathy	−0.06	0.59[a]	0.06	−0.03	0.14
Anhedonia-asociality	−0.02	0.43[c]	0.07	−0.05	0.16
Attention	−0.27	0.57[a]	0.18	0.31[b]	−0.03
Positive symptom scale					
Hallucinations	0.12	0.25	0.58[a]	0.04	−0.03
Delusions	0.32[b]	−0.04	0.53[a]	−0.06	0.22
Bizarre behavior	0.07	0.42[c]	0.28	0.35[c]	0.15
Positive thought disorder	0.21	0.11	0.54[a]	0.49[a]	0.05

[a] $p<0.001$, two-tailed.
[b] $p<0.05$, two-tailed.
[c] $p<0.01$, two-tailed.

0.005) and significantly with anergia ($r=0.40$) and thought disorder ($r=0.30$) (each $p<0.05$). This pattern of high correlations of BPRS symptoms specific to schizophrenia with anergia and thought disorder and the overall correlations of the nonspecific symptoms seems to further support the construct validity of the specific-nonspecific classification.

On the basis of scores on the Scale for the Assessment of Negative Symptoms and the Scale for the Assessment of Positive Symptoms, the patients were classified as having the positive, negative, or mixed type of schizophrenia according to Andreasen and Olsen's (7) criterion score of ≥4 (on a scale of 0–5) to indicate marked symptoms. With this criterion, seven patients were classified as having the negative, seven the positive, and 33 the mixed type. This differs significantly from the proportions reported by Andreasen and Olsen ($\chi^2=18.83$, df=2, $p<0.001$). Thus, the first hypothesis was not supported.

The principal component analysis applied to the negative and positive symptom subscale scores used the criterion of an eigenvalue ≥1; three factors accounted for 76% of the total variance. The factors were then rotated by using the Varimax solution. The rotated factor loadings are presented in table 1. All of the negative symptom subscale scores loaded highest on factor 1, with the exception of attention, which had only a moderate loading on this factor. Factor 2 was characterized by high loadings for the bizarre behavior and thought disorder subscale scores on the positive symptom scale and the highest loading for the attention subscale scores on the negative symptom scale. The hallucinations and delusions subscale scores on the positive symptom scale loaded highest on factor 3.

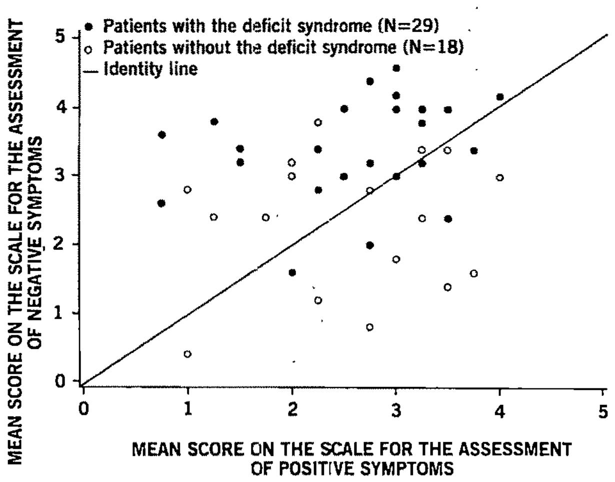
Relations Among the BPRS and the Negative and Positive Symptom Scales

The intercorrelations among the summary scores of the clinical rating scales are presented in table 2. The two methods of obtaining summary scores for the negative and positive symptom scales (average and global) were highly correlated ($r=0.95$ and $r=0.87$ for those two scales, respectively). The BPRS subscores for symptoms specific and nonspecific to schizophrenia were moderately correlated with each other, and scores on the negative and positive symptom scales were uncorrelated with each other.

We made a more detailed evaluation of the relation between the BPRS and the negative and positive symptom scales by correlating the five factor scores from the BPRS with the negative and positive symptom subscale scores (table 3). The anergia factor score from the BPRS was significantly correlated with all of the negative subscale scores and only one of the positive subscale scores. The BPRS thought disorder factor score was significantly correlated with none of the negative symptom subscale scores but with three of the four positive symptom subscale scores. The activity factor score was significantly correlated with one of the negative and two of the positive symptom subscale scores, whereas the anxiety-depression and hostility factor scores were essentially uncorrelated with the negative and positive symptom subscale scores.

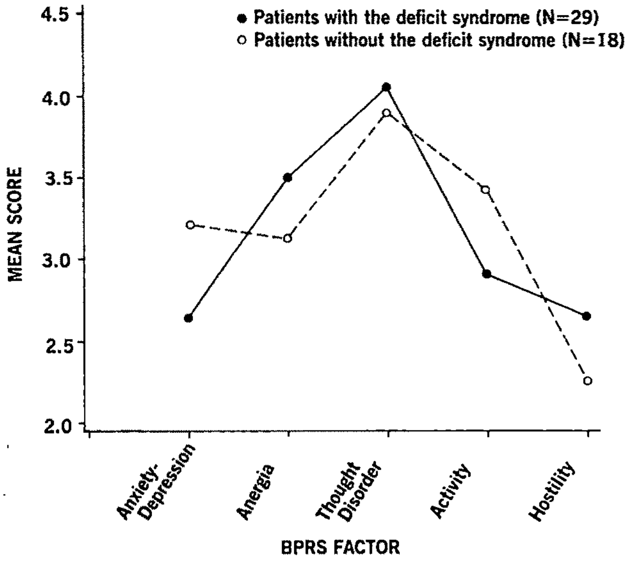
To test the hypothesis that ratings of symptoms specific to schizophrenia are correlated with negative and positive symptom severity scores, the average severity scores for all global ratings of negative and positive symptoms were correlated with scores on BPRS symptoms specific and not specific to schizophrenia. The correlation of negative/positive symptoms with BPRS symptoms specific to schizophrenia was 0.63 ($p<0.0001$) and with symptoms not specific to schizophrenia, 0.26 (n.s.). Since scores on specific and nonspecific symptoms were correlated ($r=0.44$), a partial correlation was calculated for specific symptoms with nonspecific symptoms partialed out. This correlation ($r=0.60$) was significant ($z=4.54$, $p<0.0001$). By contrast, the correlation for nonspecific, partialing out specific, was −0.02 (n.s.). Indeed, all subscale scores on the

FIGURE 1. Scatterplot and Identity Line for Mean Scores of 47[a] Schizophrenic Patients With or Without the Deficit Syndrome on Negative and Positive Symptom Scales



[a]Some circles represent more than one patient.

FIGURE 2. Mean Scores of 47 Schizophrenic Patients With or Without the Deficit Syndrome on Five BPRS Factors



negative symptom scale were correlated significantly (at the 0.05 level, one-tailed) with scores on symptoms specific to schizophrenia (correlations ranging from 0.27 for anhedonia to 0.51 for thought disorder), whereas all except two subscale scores were uncorrelated with symptoms not specific to schizophrenia (correlations ranging from −0.04 for affect to 0.19 for delusions). The exceptions were $r=0.37$ for bizarre behavior and $r=0.35$ for thought disorder (each $p<0.01$). Thus, scores on the BPRS items that include symptoms considered specific to schizophrenia were correlated with scores on a scale that is aimed at quantifying the severity of schizophrenia-related symptoms.

Relations With the Deficit-Nondeficit Classification

Of the 47 patients, 29 (62%) were classified as having the deficit syndrome and 18 (38%) as not having the deficit syndrome. These proportions deviate significantly ($\chi^2=34.53$, df=1, $p<0.0001$) from those reported for 103 patients by Carpenter et al. (8): 15 (15%) with deficit and 88 (85%) without deficit or uncertain. A scatterplot of classifications according to the negative and positive symptom scales (figure 1) shows that patients with and without the deficit syndrome were distributed across the range of positive symptom scores. As expected, on the negative symptom scale the patients with the deficit syndrome aggregated toward the higher scores and the patients without the deficit syndrome toward the lower scores.

Statistical analyses contrasting patients with and without the deficit syndrome suggested additional effects. Patients with the syndrome did not have higher overall BPRS scores, but the division of the BPRS items into the five factors yielded a significant Factor by Deficit-Nondeficit interaction ($F=2.58$, df=4, 180, $p<0.05$) (figure 2). Patients with the deficit syndrome scored higher on the triad of anergia, thought disorder, and hostility relative to the patients without the syndrome, who scored higher on anxiety-depression and activity. The deficit-nondeficit classification was also associated with the specific-nonspecific dimension of the BPRS ($F=5.07$, df=1, 45, $p<0.05$). The scores of patients with the deficit syndrome showed a steeper gradient for items specific to than not specific to schizophrenia (figure 3). As expected from the definition of deficit and nondeficit, deficit syndrome patients had higher scores on the negative symptom subscales. They did not differ from the patients without the syndrome on the positive symptom scale (Deficit-Nondeficit by Negative-Positive interaction, $F=12.14$, df=1, 45, $p<0.001$) (figure 4).

To evaluate formally the existence of subtypes, the intercorrelations among the summary scores for the negative and positive symptom scales and the BPRS items specific to schizophrenia were subjected to a hierarchical cluster analysis procedure using Ward's method (SAS Cluster procedure). Three clusters emerged, with nine patients in cluster 1 (high scores on specific and positive symptoms, low scores on negative symptoms), 14 in cluster 2 (high scores on all three), and 24 in cluster 3 (low scores on specific, high on positive and negative). The distribution of patients with and without the deficit syndrome was significantly different in these clusters ($\chi^2=7.87$, df=2, $p=0.02$). The Cochran-Mantel-Haenszel statistic for general association was 7.71, $p=0.02$. In cluster 1 there were two patients with and seven without the deficit syndrome; in cluster 2, 11 and three; and in cluster 3, 16 and eight. This distribution indicated a significant difference between clusters 1 and 2 ($\chi^2=7.08$, df=1, $p=0.008$; corrected for continuity, $\chi^2=$

FIGURE 3. Mean Scores of 47 Schizophrenic Patients With or Without the Deficit Syndrome on BPRS Items Specific to Schizophrenia and Not Specific to Schizophrenia

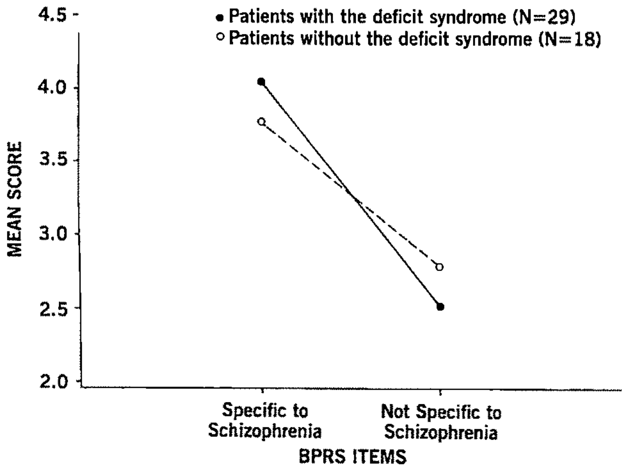
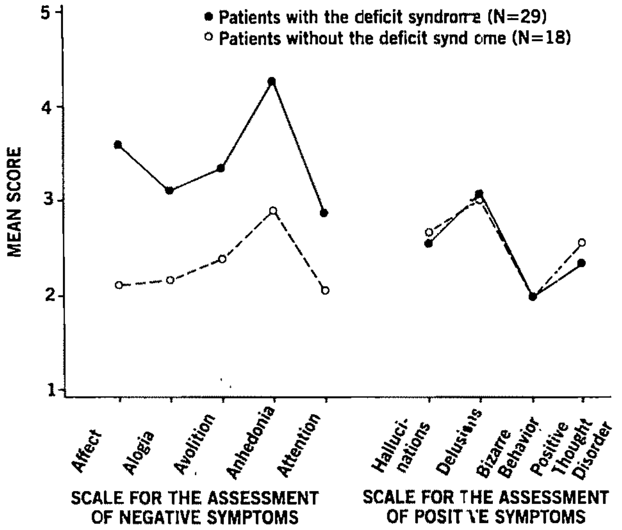


FIGURE 4. Mean Scores of 47 Schizophrenic Patients With or Without the Deficit Syndrome on Subscales of Negative and Positive Symptom Scales



4.97, p=0.03) and between clusters 1 and 3 (χ^2=5.22, df=1, p=0.02; corrected for continuity, χ^2=5.39, p=0.02), but not between clusters 2 and 3 (χ^2<1).

DISCUSSION

Use of the BPRS and the scales for negative and positive symptoms and examination of their relation to the deficit-nondeficit classification helped clarify some issues related to the phenomenology of schizophrenia. Concerning the BPRS, the scores on the five traditional factors suggested that the subjects were characterized by symptoms which are the hallmark of schizophrenia, such as thought disorder. The division of the BPRS into symptoms specific and not specific to schizophrenia (3) also seems to have received construct validation as an approach to characterizing schizophrenic patients. In this sample, diagnosed according to *DSM-III-R* criteria, all but two patients had higher specific symptom scores than nonspecific symptom scores. Furthermore, the specific symptom scores were correlated most highly with thought disorder and anergia, whereas the nonspecific symptom scores were correlated with all factors and most highly with the anxiety-depression factor, which is not considered a hallmark of schizophrenia. The validity of this division is further suggested by the finding, as hypothesized, of a correlation of specific and not of nonspecific symptom scores with the negative and positive symptom scale scores, which were designed to quantify the range of symptoms of schizophrenia.

For the Scale for the Assessment of Negative Symptoms and the Scale for the Assessment of Positive Symptoms, the summary scores obtained by global ratings of symptom clusters were highly correlated with the average scores for individual items. For all patients, global ratings were higher than averaged ratings. The low correlation between negative symptom scores and positive symptom scores is consistent with earlier results (7) and supports the notion that they measure different aspects of psychopathology associated with schizophrenia. On the other hand, the sample was not equally divided into three groups with positive, mixed, and negative symptoms. The extreme groups were underrepresented in comparison to those in Andreasen and Olsen's report (7); hence, the hypothesis that the majority of patients with schizophrenia can be classified as having the positive or negative type was not supported. This raises doubts about the utility of the positive-negative dichotomy, as defined by these scales, as the sole means of identifying distinct major subtypes of schizophrenia. Other cutoff points could be considered, and the stability of the classification can be examined in longitudinal studies.

The different clinical scales seem to measure related but not overlapping dimensions. This is suggested by the moderate correlations among scores on the negative and positive symptom scales and the BPRS. While the specific and nonspecific symptom measures of the BPRS are helpful in characterizing patients with schizophrenia relative to other patient populations, the specific symptom measure yields only an index of overall severity of schizophrenia. The negative and positive symptom scale items cover a comprehensive range of symptoms, and other groupings of symptoms may emerge beyond the negative-positive dimension. The factor analysis of the negative and positive symptom scores suggests that while, for the most part, the division suggested by Andreasen and Olsen is valid, there may be additional divisions of symptoms. Attention, which is an item on the negative symptom scale, shared substantial loading with the other items on that scale but had a higher loading on a factor containing two positive symptom scale items (bizarre behavior and positive formal thought disorder). This triad was most highly correlated with the activity factor score of the BPRS and may suggest a division of the positive symptom scales into two dimensions, one of which may incorporate the attention item of the negative symptom scale. This finding should be replicated to warrant further discussion.

The larger proportion of patients with the deficit syndrome in this sample, compared to Carpenter et al.'s (8), may reflect either the more severely disturbed group we were studying or the more lax criteria for categorizing patients as having the deficit syndrome. We followed Carpenter et al.'s criteria as described and believe that all the patients we classified as having the syndrome manifested at least two of the five features required for that classification (flattened or restricted affect, anhedonia, poverty of speech, lack of sense of purpose, and lack of social drive). Our deficit syndrome patients differed from those without the syndrome on several measures, supporting the validity of this classification. They had more of the BPRS symptoms specific to schizophrenia and fewer of the nonspecific symptoms, and they had more symptoms on the negative symptom scale. This pattern of results suggests that the positive-negative and deficit-nondeficit dimensions have partial overlap in that, as intended by Carpenter et al. (8), deficit syndrome patients are characterized by more negative symptoms.

The utility of the deficit-nondeficit classification is further supported by the cluster analysis of the clinical scale scores. The differences in the distribution of patients with and without the deficit syndrome in the three clusters indicate that this dichotomy is useful in depicting subtypes. While patients without the deficit syndrome were characterized by low scores on the negative symptom scale but high scores on positive and schizophrenia-specific symptoms, patients with the deficit syndrome were overrepresented in the group with severe negative, positive, and schizophrenia-specific symptoms. These patients seemed sicker overall. A third cluster suggested by the data were patients with high scores on negative and positive symptoms but relatively lower scores on schizophrenia-specific symptoms. In this group, too, the majority of the patients had the deficit syndrome. This requires further evaluation with larger samples.

Whether different pathophysiology underlies these patient groups can be determined by neuroimaging studies. A subsample of the patients reported here have been studied with magnetic resonance imaging and positron emission tomography procedures. Some predictions can be made on underlying pathology in view of Hughlings Jackson's (14) hypothesis that negative symptoms emanate from structural brain lesions, whereas positive symptoms reflect disturbed physiologic activity. The patients whose scores aggregate in the high range on both the negative and positive symptom scales are likely to have the greatest number of structural and physiologic abnormalities, whereas the group scoring high on positive symptoms and low on negative symptoms should have primarily physiologic abnormalities. There is already some evidence that symptom type and severity are related to neuroanatomic and neurophysiologic parameters (15).

The findings in this study have limited generalizability to patients with schizophrenia who do not meet a set of exclusion criteria. We chose rather stringent criteria, since our research focuses on the study of brain function with relatively new methods. Thus, we aim to reduce the potential contribution of other factors that may affect regional brain structure and function and complicate the interpretability of the data on this heterogeneous disorder. This emphasis on establishing sensitivity of methods to the presence of schizophrenia should be supplemented at a later stage by studies establishing the specificity of findings.

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Familial, Obstetric, and Other Clinical Correlates of Minor Physical Anomalies in Schizophrenia

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Objective: This study investigated possible antecedents of minor physical anomalies in schizophrenia, particularly in terms of obstetric and genetic factors, and demographic, clinical and cognitive correlates of such anomalies in schizophrenia. Method: Forty-one outpatients satisfying the DSM-III *criteria for schizophrenia were examined for minor physical anomalies by using the Waldrop scale. These subjects were drawn from a group of 45 such patients whose cognitive function had been previously evaluated with Trail Making Tests A and B and whose biological mothers had been interviewed for any history of obstetric complications or family history of schizophrenia. Results: Linear multiple regression analysis showed that higher scores for minor physical anomalies were associated with impaired cognitive flexibility on Trail Making Test B, family history of schizophrenia in a first-degree relative, maternal history of obstetric complications, smaller number of siblings, later position in the birth order, and male sex. A family history of schizophrenia was particularly associated with abnormalities of the mouth. The association between minor physical anomalies in the patients and obstetric complications in their mothers appeared to be confined to instances in which the mother had a history of bleeding in early pregnancy. Conclusions: Minor physical anomalies indicate early dysmorphogenesis in schizophrenia, particularly in males, which appears to be associated more reliably with genetic rather than obstetric factors and with cognitive impairment.*

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Current perspectives on schizophrenia as a neurodevelopmental disorder propose that unspecified events act somewhere in the prenatal or perinatal period to bring about, through neuronal dysplasia, a failure to attain fundamental development of cerebral structure and function. The interaction between such a static lesion of very early origin and "normal" processes of neuronal maturation then results in perhaps subtle premorbid features and, subsequently, in the emergence of more typical diagnostic symptoms (1, 2). Such notions have stimulated both empirical studies and etiological theorizing (3–6).

One possibly important clue to developmental abnormality in schizophrenia is the association of schizophrenia with minor physical anomalies. These slight anatomical abnormalities are believed to arise because of events that occur during the early stages of embryonic and fetal growth, possibly but not incontrovertibly during the first trimester, when most essential ectodermal derivatives develop their basic structure (7). It has been reported in three studies (8–10) that these anomalies are more evident in schizophrenic patients (prominent in 31%–75% of subjects) than in normal individuals (prominent in 0%–13% of subjects). However, the few studies of schizophrenia that have sought clinical correlates of minor physical anomalies have produced inconsistent findings in relation to age at onset, cognitive performance, and premorbid functioning (9–11), and the possible antecedents of these abnormalities remain essentially unexplored.

Since minor physical anomalies are evident in some patients who have experienced prenatal insults (7), obstetric complications, which have been shown to occur in excess in the mothers of patients with schizophrenia (12, 13), might be antecedent factors. Alternatively, since minor physical anomalies are widely recognized in genetically determined neurodevelopmental disorders such as Down's syndrome (7), genetic factors, which are known to be important in the etiology of schizophrenia (14, 15), might be antecedents. The pur-

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TABLE 1. Characteristics of 41 Schizophrenic Patients Divided Into Two Groups on the Basis of Their Waldrop Scale Scores for Minor Physical Anomalies

	Patient Group			
	Score≤4 (N=30)		Score>4 (N=11)	
Characteristic	Mean	SD	Mean	SD
Age (years)	32.3	8.1	34.0	5.6
Age at onset (years)	22.9	6.1	23.8	3.8
Birth order (firstborn=1)	3.1	2.1	2.8	1.9
Number of siblings	4.9	2.6	3.7	2.2
Trail Making Test A (seconds)	48.2	16.6	59.4	34.7
Trail Making Test B (seconds)	107.4	40.1	155.5	88.3

pose of the present study was to quantify minor physical anomalies in a group of schizophrenic patients, to seek relationships with such putative antecedents, and to examine further their clinical correlates. A particular hypothesis was that minor physical anomalies might be overrepresented in patients whose mothers had experienced complications during pregnancy.

METHOD

The subjects of this study were 41 outpatients, ranging in age from 20 to 48 years, who were attending an outpatient clinic in Dublin. They satisfied the *DSM-III* criteria for schizophrenia on the basis of case note review and, where necessary, clinical interview by the study diagnostician (16), and they gave informed consent before participating in the study. The 41 subjects were drawn from a group of 45 patients, each of whom had a living biological mother who was willing to be interviewed in relation to the patient and his or her family. We had studied this group (16) for any associations of cognitive function with a history of obstetric complications in the mother, a family history of psychiatric disorder, and vulnerability of the patient to tardive dyskinesia. Cognitive function was evaluated as the time (in seconds) taken to complete Trail Making Tests A and B (17), two visual scanning, visuomotor coordination, and cognitive flexibility tasks of known utility for such younger outpatient populations (18, 19). About 18 months after the initial patient examinations and interviews with the mothers, and without reference to the records of the previous assessments, the same investigator reexamined the patients for minor physical anomalies. Over the intervening period, two patients had committed suicide and two could not be traced.

Patients were examined for minor physical anomalies by using the Waldrop scale (20, 21), which assesses morphological abnormalities of six body regions: the head, eyes, mouth, ears, hands, and feet. As in other studies that have used this scale (11, 20), measurement of head circumference was suspended because of the lack of normative data. Although in our experience the Waldrop scale is not sensitive to the entire range of minor physical anomalies encountered, it represents the prevailing standard pending development of an improved scale.

The biological mother of each patient had been interviewed in relation to her obstetric history and family psychiatric history as described previously (16). Briefly, she was interviewed first about her obstetric history when she was pregnant with the patient. A history of obstetric complications was specified as the presence of at least one "definite" complication as defined by the scale of Lewis et al. (22). We have recently validated the application of this scale to information obtained by maternal recall in a group of 21 patients for whom maternity hospital records were also available (23). Each mother was asked whether she had abused alcohol or had taken any prescribed or illicit drugs during her pregnancy; there were no reports of such use. Second, a family tree of at least all first- and second-degree relatives of the patient was constructed, and for each relative a life history was taken for specification of any psychiatric disorder. It has been reported that this procedure greatly increases the sensitivity of the family history method (24). A positive family history was defined as having a first-degree relative with schizophrenia according to the Family History Research Diagnostic Criteria (25). We also ascertained, from clinical records and the interview with the mother, the patient's age at onset of schizophrenia (defined as first presentation to a psychiatric service), birth order (1=firstborn), and number of siblings.

To examine the relation of variables to total score on the Waldrop scale, data were analyzed by linear multiple regression with a "t-directed search" method to determine the best or most parsimonious model (26). Subsequent univariate comparisons were made with Student's t test or Fisher's exact probability test (two-tailed).

RESULTS

The mean±SD score on the Waldrop scale for this patient group was 2.8±2.8; individual scores exceeded 4 for 11 of the 41 patients. A cutoff score of greater than 4 has been used in several previous studies of minor physical anomalies (8, 9) and is based on the range of scores encountered in normal subjects. In the subgroup with Waldrop scale scores of 4 or less (N=30), there were 16 male patients and 14 female patients. Nine (30%) of the patients in this subgroup had family histories of schizophrenia, and 10 (33%) had mothers with histories of obstetric complications. In the subgroup with Waldrop scale scores greater than 4 (N=11), there were nine male and two female patients. Six (55%) had family histories of schizophrenia, and four (36%) had mothers who had had complications during pregnancy. Demographic and neuropsychological variables for the two subgroups are given in table 1.

Coefficients for the final linear multiple regression model are shown in table 2, where each of these coefficients has an absolute t value in excess of the 95% point of Student's t distribution. Higher scores on the Waldrop scale were associated with poorer performance on Trail Making Test B, positive family history of schizophrenia, history of obstetric complications in the mother, smaller number of siblings, later position in the birth order, and male sex. The goodness of fit of the final regression model was satisfactory.

Because of the apparent relationships between minor physical anomalies and both family history of schizophrenia and history of obstetric complications in the mother, patients were subdivided into those to whom one but not the other, or neither, of these situations applied. Fourteen patients had neither a family history of schizophrenia nor a mother who had had obstetric complications (mean±SD Waldrop score=1.8±2.3); 13 had family histories of schizophrenia but did not have mothers who had had obstetric complications (mean score=3.5±3.0) (t=1.72, df=25, $p<0.10$, for the comparison); and 12 had mothers who had had obstetric complications but there was no family history of schizophrenia (mean score=2.9±2.6). Only two patients had both the family history and the maternal history. This number was too small for meaningful analysis.

The patients who had family histories of schizophrenia but whose mothers had not had obstetric complications tended to have more body regions affected by minor physical anomalies than did the patients with neither the family history nor the maternal history (2.7±2.2 and 1.3±1.5 regions, respectively; t=1.91, df=24, $p<0.10$), while the patients whose mothers had had obstetric complications but who did not have family histories of schizophrenia had an intermediate number of body regions affected (2.1±1.7). Furthermore, the patients with family histories of schizophrenia whose mothers had had no obstetric complications were more likely to show minor physical anomalies of the mouth (present in eight of 13 such patients) than were the patients without the family history (mouth anomalies present in seven of 26 such patients: four of 14 without the maternal history and three of 12 with the maternal history) ($p<0.05$, Fisher's exact probability test). Trends toward more frequent anomalies of the head and eyes in this same patient group failed to attain statistical significance.

On reexamination of the mothers' recall of obstetric complications, we found that scores on the Waldrop scale for the four patients whose mothers reported, among other things, a history of bleeding in early pregnancy (two with bleeding at 9 weeks, one at 25 weeks, and one at an unspecified time) significantly exceeded the scores for the 10 patients whose mothers reported obstetric complications that did not include such an event (mean±SD scores=5.8±3.4 and 2.1±2.3, respectively; t=2.34, df=12, $p<0.05$). The latter score was virtually identical to that for the 14 patients who had neither a mother with obstetric complications nor a family history of schizophrenia.

TABLE 2. Linear Multiple Regression Model for Correlates of Waldrop Scale Scores for Minor Physical Anomalies in 41 Schizophrenic Patients[a]

Variable	Beta	SE	t	p
Trail Making Test B	0.019	0.006	3.10	<0.01
Family history of schizophrenia	2.355	0.779	3.02	<0.01
Obstetric complications in the mother	2.372	0.800	2.97	<0.01
Number of siblings	−0.749	0.242	−3.10	<0.01
Birth order	0.814	0.304	2.68	<0.02
Sex	−1.751	0.771	−2.27	<0.05
Constant	0.502			

[a] R^2=50.6%, adjusted R^2=41.9%; residual df=34.

DISCUSSION

Since the available evidence indicates that minor physical anomalies arise through processes which act during the early stages of embryonic and fetal life (7), the overrepresentation of these anomalies in patients with schizophrenia (8–10) supports the view that this disorder is related to factors operating early in development (1–6). Thus, identification of antecedents of minor physical anomalies might provide important clues to the causes of neurodevelopmental abnormality in schizophrenia.

There was a significant association between minor physical anomalies in the patients and obstetric complications in their mothers. Obstetric complications are known to occur to excess in the mothers of patients with schizophrenia (12, 13), and it is established that anatomical malformations can sometimes arise from insults to the fetus in utero (7). Problematically, the great majority of obstetric complications recorded from mothers' recall or from maternity hospital records (e.g., cord prolapse, abnormal presentation, high forceps delivery, cesarean section, and postmaturity [22, 23]) concern the perinatal period, whereas minor physical anomalies are believed to reflect considerably earlier events. However, separating patients with maternal histories of obstetric complications into two groups on the basis of whether or not the complications included bleeding in early pregnancy (the one complication reliably reported to occur considerably earlier in the course of pregnancy) indicated that the association between mothers' obstetric complications and minor physical anomalies in their children depended substantially on a history of such bleeding. It appeared to have little relation to other, predominantly perinatal events. Furthermore, this relationship need not be one of cause and effect (27) and could reflect the failure of the uterus to follow through on the threat to expel a conceptus with a preexisting malformation (28).

In this regard, we found minor physical anomalies to be strongly associated with a family history of schizophrenia. Thus, to the extent that such familial association can be assumed to reflect hereditary processes, the genetic factors known to operate in the etiology of schizophrenia (14, 15) also appear to have a critical association with embryonic/fetal dysmorphogenesis. This would be consistent with a substantial body of evidence that most previously recognized patterns of human anatomical malformation, both major and minor, have a genetic basis and are associated with varying forms and severities of nervous system disorder (7). Since a recent investigation (10) noted that abnormalities of the mouth are the most common minor physical anomalies in schizophrenia, the present study explored their topography in relation to these putative antecedents. The principal finding was both a greater number of body regions affected by minor physical anomalies and a higher prevalence of mouth abnormalities in the subgroup of patients who had family histories of schizophrenia but whose mothers had not had any obstetric complications. This relationship suggests that familial/genetic factors may determine not only the development of minor physical anomalies but also a particular topography of developmental abnormality. More speculatively, it might suggest that the genetic factors relevant to schizophrenia are related in some way to those which determine oral morphogenesis.

Higher scores for minor physical anomalies were found to be associated with poorer neuropsychological test performance. Previously, an "impairment index," derived from a short battery of neuropsychological tasks that included the Trail Making Test, was found to be unrelated to Waldrop scale score (9). Also, Waldrop scale score has been reported to be unassociated with measures of vigilance, selective attention, and orientation (10). However, the selective association we found was with poor performance on Trail Making Test B (rather than A), which places an additional demand on cognitive flexibility; this suggests some link between minor anomalies of body morphology and at least this aspect of cerebral dysfunction.

Although one group of investigators (10, 11) reported that minor physical anomalies are associated with earlier age at onset of schizophrenia, we could find no evidence for such an association, either in all the patients or selectively in the male patients. However, demographic and procedural differences between our study and the one reported by that group—in recording age of outpatients at first presentation to a psychiatric service as opposed to age of inpatients at first hospitalization—appear to vitiate attempts to compare them directly. Others have also failed to find any relation between minor physical anomalies and age at onset (9).

In our study, minor physical anomalies were more evident in male patients. Although a recent study (10) did not note any sex differences in Waldrop scale score, that study involved a predominantly male group of state hospital inpatients rather than a more mixed outpatient group such as we studied, and thus the findings may not be comparable. The male brain is generally more vulnerable to early insults (2, 29), and male sex appears to be associated with an unfavorable prognosis in schizophrenia (30, 31); in a recent family study, neurological abnormalities appeared more likely to lead to schizophrenia in male subjects than in female subjects (32).

We also found that scores on the Waldrop scale were greater for patients having a smaller number of siblings and a later position in the birth order of those siblings. This association of characteristics might arise if patients having the more evident minor physical anomalies were among the later born of a modest number of siblings because of greater maternal and/or paternal age at their conception. Greater parental age is associated with a greater likelihood of certain chromosomal abnormalities known to result in malformations (7), and its status as a possible risk factor for schizophrenia has been reconsidered in the past few years (33). However, we could find no obvious differences in either maternal or paternal age between patients with and without minor physical anomalies. Alternatively, patients with the more evident minor physical anomalies might be among the last born of a modest number of siblings because of defective parental fertility that arose through other, as yet unspecified, endogenous or environmental factors. These family indices may be a proxy for some more fundamental process or processes that regulate aspects of development and biological function.

Correlates of minor physical anomalies identified in this study appear to show some parallelism with other neurodevelopmental perspectives on schizophrenia. Thus, evidence has been offered for an "inherited, congenital neurointegrative defect" ("pandevelopmental retardation" [34] or "pandysmaturation" [35]) in schizophrenia that is more related to genetic risk for schizophrenia than to obstetric complications and is associated with cognitive disorder. Similarly, a recent study (36) has presented computed tomographic evidence for "multisite neural developmental deficits" in cerebral morphology that were also more related to genetic risk for schizophrenia than to obstetric complications in the mother. Such complications may be more associated with other abnormalities in cerebral morphology, particularly increased ventricule size (13, 36).

These results provide initial information on the relation of minor physical anomalies and developmental abnormality in schizophrenia to putative antecedent factors of etiological significance and suggest a greater role for genetic than for obstetric factors. Clearly, any specificity of such findings to schizophrenia cannot be determined in the absence of comparable data involving other diagnostic groups. However, our data indicate the potential of this approach for clarifying further the nature of early events and resultant neurodevelopmental anomalies that appear to be involved in the subsequent emergence of this disorder.

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Relation of CSF Neurotensin Concentrations to Symptoms and Drug Response of Psychotic Patients

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Objective: The authors investigated the putative endogenous antipsychotic neurotensin in relation to both psychotic symptoms and patterns of response during treatment with an antipsychotic drug. Method: Twenty recently admitted patients with mood-incongruent psychoses underwent 1) interviews with the Schedule for Affective Disorders and Schizophrenia for diagnostic evaluation and symptom profiles, 2) drug-free baseline measurements of CSF neurotensin and homovanillic acid, and 3) close monitoring of a therapeutic trial of haloperidol to determine latency of antipsychotic response. Results: A relative deficiency in CSF neurotensin was found in a subgroup of psychotic women whose clinical response to haloperidol was delayed for 11 to 35 days after initiation of the neuroleptic. These patients had greater thought disorder, delusions-hallucinations, behavioral disorganization, and impaired functioning than did psychotic patients with higher CSF concentrations of neurotensin. Neurotensin concentrations increased during treatment with haloperidol. Conclusions: The study provides further evidence that there is diminished availability of neurotensin in some psychotic patients, with increases in neurotensin early in neuroleptic treatment. Exploration of neurotensin receptor agonists as a potentially novel class of antipsychotic compounds is suggested.

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Neurotensin, an endogenous tridecapeptide, is found in the CNS. Its highest concentrations are in the hypothalamus, the substantia nigra, the periaqueductal gray matter, and the limbic system, including the nucleus accumbens, septum, and amygdala (1, 2). High-affinity binding sites for neurotensin—putative neurotensin receptors—have been identified; these are also distributed heterogeneously in the mammalian CNS (3).

A series of investigations have implicated neurotensin in the modulation of dopamine neurotransmission (4, 5). Mesencephalic dopamine perikarya are activated by direct microinjection of neurotensin (6). Application of neurotensin to brain regions containing mesocorticolimbic dopamine terminals and dopamine receptors has behavioral effects the opposite of those seen after administration of dopamine in these regions, although neurotensin does not affect dopamine D_2 binding kinetics (7, 8).

Many of the effects of centrally administered neurotensin appear to be similar to those of classic neuroleptic drugs. Although neurotensin does not bind to D_2 receptors (as do classic neuroleptic drugs), it seems to reverse the ultimate effects of signal transduction initiated at D_2 receptors by dopamine. Like antipsychotic drugs, neurotensin induces catalepsy and inhibits discrete trial-conditioned avoidance behavior without sedation (9, 10). Like neuroleptics, neurotensin increases the metabolic activity of presynaptic dopamine neurons (11). These findings suggest that neurotensin may have neuroleptic-like activity within the CNS. The data have been reviewed by Levant and Nemeroff (12).

In a group of schizophrenic patients, Widerlov et al. (13) found a subgroup who had markedly lower CSF concentrations of neurotensin when they were in the drug-free state. In this subgroup, although age, course of illness, baseline global psychopathology, and degree of eventual improvement after taking neuroleptics were not correlated with neurotensin levels, 75% of the women but only 35% of the men had the lower

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neurotensin values. No difference in neurotensin level was found between female and male control subjects. Treatment with neuroleptics was found to increase CSF neurotensin in the subgroup of patients with low pretreatment concentrations, but in the patients who did not have low levels of neurotensin when they were drug free, levels did not change after neuroleptic treatment. Two other studies (14, 15) have also revealed lower neurotensin concentrations in the CSF of drug-free schizophrenic patients.

The purpose of this investigation was to study still another group of psychotic patients for deficits in CSF neurotensin and to characterize more carefully the subgroup who have low neurotensin levels. To do this we used *DSM-III* diagnostic criteria, profiles of specific schizophrenic symptoms (delusions-hallucinations, formal thought disorder, behavioral disorganization, and impaired functioning), baseline CSF homovanillic acid (HVA) levels, and differential patterns of response to drug treatment.

METHOD

Twenty patients with mood-incongruent psychoses and six comparison subjects of similar age entered the study after giving informed consent. Neither the patients nor the comparison subjects had diagnosable medical illness, and none was taking medication for medical illness. The mean±SD age of the psychotic patients was 27.7±6.9 years (range=19–44); 50% of the group were female. Although the patients were admitted to inpatient services immediately before the study began, their present episodes of psychotic illness had lasted from 1 to 260 weeks (mean±SD=70.3±91.0) in ambulatory status; it had been 2 weeks to 15 years (mean±SD=4.8±4.0 years) since the onset of their first psychotic episodes. After the patients had been interviewed with the Schedule for Affective Disorders and Schizophrenia (SADS) (16), which was supplemented with information from collateral sources, they were given the following diagnoses according to *DSM-III*: schizophrenia (N=15), schizophreniform disorder (N=2), and psychotic, mood-incongruent affective disorder (N=3). We used the SADS summary scales (17) to develop a symptom profile for each patient.

The patients had been free of neuroleptic drugs for at least 2 weeks before the initial CSF examinations. Lorazepam, in doses of 2–8 mg/day, was used to control behavior during the neuroleptic-free study period.

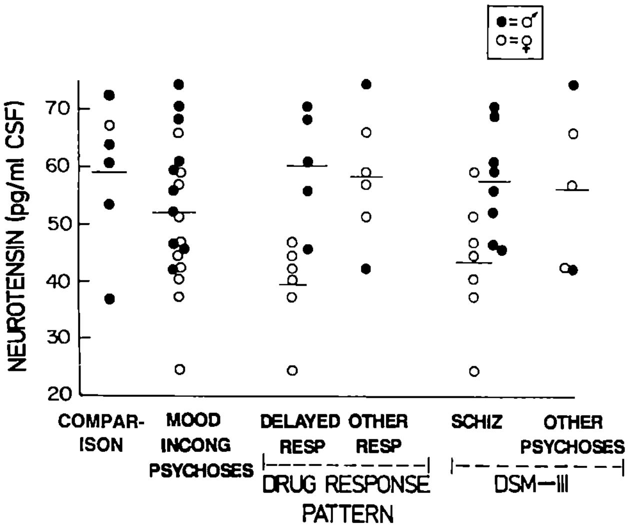
At the end of the neuroleptic-free period, between 8:00 and 9:00 a.m., a lumbar tap at the L4–L5 level was performed with the patient in the lateral decubitus position. CSF was withdrawn in 1-ml fractions, which were immediately immersed in dry ice and ethanol at the bedside. The CSF samples were refrigerated at −70 °C until transported on dry ice for assay of neurotensin and HVA.

The neurotensin assays were performed as previously described (13–15) without knowledge of the diagnoses of the patients. The samples of CSF were thawed, and duplicate 200-μl aliquots were placed in borosilicate glass tubes, lyophilized, and reconstituted in 200 μl of radioimmunoassay buffer. A standard curve of synthetic neurotensin was composed of unlabeled neurotensin serially diluted in artificial CSF (256 to 1.25 pg of neurotensin per milliliter), which was lyophilized and also reconstituted in 200 μl of buffer. A primary neurotensin polyclonal antibody was added to the tubes to a final concentration of 1:12,000. This antiserum recognizes the midportion of the neurotensin molecule (Lys-Pro-Arg) with an IC_{50} of 80 pg and a maximum sensitivity of 1.25 pg per tube. [^{125}I]neurotensin was prepared by the chloramine-T/metabisulfate reaction and purified on a carboxymethylcellulose column. Approximately 20,000 counts per minute were added to the assay after the primary antiserum and samples had been incubated at 4 °C for 24 hours. The following day, goat antirabbit second antibody was added to precipitate bound radioactivity for 24 hours at 4 °C. The tubes were then centrifuged, supernatants aspirated, and pellets counted on an LKB Rackgamma 1274 gamma counter. Results are reported as picograms of neurotensin per milliliter of CSF. The neurotensin assay reported here had a mean±SD coefficient of variation of 14.2%±7.9% (N=6) at a range of 40–60 pg of neurotensin per milliliter of CSF. Neurotensin assays were done on milliliters 7 and 8 of the lumbar CSF. HVA assays were done by high-pressure liquid chromatography (18) on CSF milliliters 5 and 6.

We systematically examined drug response patterns in 19 of the 20 psychotic patients. Psychotic symptoms were scored serially on the modified New Haven Schizophrenic Index (19), which was administered at baseline and at least three times weekly throughout drug treatment. The standardized protocol (20) first evaluated the potential antipsychotic effects of lithium alone during a 2-week treatment period. Patients classified as lithium responders showed at least a 35% reduction of baseline psychosis scores by day 14 of the lithium trial and went on to be discharged essentially symptom free (more than a 90% reduction of psychosis scores) on a regimen of lithium alone, without any exposure to neuroleptics. Patients classified as lithium nonresponders were subsequently started on haloperidol. Patients who experienced a 55% reduction of psychotic symptoms in the first week of haloperidol treatment were designated as rapid neuroleptic responders. Patients who responded to haloperidol but in whom a 55% reduction of psychotic symptoms did not occur until more than 7 days after the initiation of the drug were designated as delayed neuroleptic responders. A small group of patients who responded neither to lithium nor to haloperidol were designated as residual responders or nonresponders (20).

Four of the patients underwent a second lumbar puncture early in the course of drug treatment. The second CSF sample from a patient with a schizophren-

FIGURE 1. CSF Neurotensin Levels of 20 Psychotic Patients and Six Comparison Subjects at Baseline and of the Patients in Relation to Drug Response Patterns and *DSM-III* Diagnoses



iform disorder was obtained on day 14 of lithium treatment after an antipsychotic response to lithium alone. Three schizophrenic patients who did not respond to lithium also had second CSF samples withdrawn 7–14 days after initiation of treatment with haloperidol but, in each case, before achieving a 55% reduction of psychotic symptoms.

We used Mann-Whitney U tests to test the significance of differences when inspection of the data suggested abnormal distributions. Otherwise, we used Student's t test in the data analyses.

RESULTS

The total group of 20 patients with mood-incongruent psychoses evidenced only a modest trend toward neurotensin levels lower than those of the comparison subjects (mean±SD=52.4±12.5 and 59.1±12.6 pg/ml, respectively; Mann-Whitney z=1.10, p=0.14, one-tailed). One of the comparison subjects, who had no evidence of psychiatric disease in himself or in his family, had a lower neurotensin level than all but one of the patients. However, the 10 psychotic women appeared to have lower neurotensin levels than the 10 psychotic men (mean±SD=47.1±12.0 and 57.7±11.2 pg/ml, respectively; Mann-Whitney z=1.89, p=0.06, two-tailed) (figure 1). There was no significant association between age or length of illness (years since first episode) and neurotensin level in the total group of psychotic patients (r=0.06 and r=0.30, respectively) or in the male and female patients separately.

Profiles of schizophrenia-related symptoms, constructed from SADS summary scores, were available for 18 of the 20 patients for the present episode of psychosis. The profiles indicated that the patients who had neurotensin levels below the 40th percentile (more than one standard deviation below the mean for the comparison subjects) manifested more severe typically schizophrenic psychopathology than did patients with higher neurotensin concentrations. During the index episode of psychosis, the patients with neurotensin below the 40th percentile (N=8), compared to the patients with higher neurotensin levels (N=10), had higher scores on formal thought disorder (mean±SD=30.1±14.3 and 11.8±12.9, respectively; t=2.23, df=16, p=0.01), behavioral disorganization (35.6±14.0 and 19.7±14.9; t=2.23, df=16, p=0.04), and impaired functioning (73.8±15.1 and 54.0±23.2; t=2.08, df=16, p=0.05). The patients with lower neurotensin concentrations also showed a trend toward higher scores on delusions-hallucinations during the entire psychotic episode (66.4±18.4 and 51.4±16.4, respectively; t=1.84, df=16, p=0.08) and significantly higher scores on delusions-hallucinations during the week preceding the lumbar tap (49.6±13.6 and 32.3±11.9; t=2.87, df=16, p=0.01). Although there was an excess of women in the group with low neurotensin levels (five women and three men), scores on the SADS summary items of formal thought disorder, behavioral disorganization, impaired functioning, and delusions-hallucinations during the episode did not differ significantly between the total group of psychotic women and the total group of psychotic men (t=0.05, t=0.24, t=1.70, t=0.92, respectively, df=16, p>0.10). It should also be noted that no trends toward differences in affective symptoms (either depressive or manic) or differences in anxiety profiles between the group with lower neurotensin levels and the remainder of the patients emerged.

When we grouped the psychotic patients according to their *DSM-III* diagnoses, we found that the neurotensin levels of the 15 patients with schizophrenia did not differ from those of the other patients (mean±SD=51.0±12.1 and 56.4±14.2 pg/ml, respectively; Mann-Whitney z=0.57, p=0.56) (figure 1). However, the seven schizophrenic women had a significantly lower neurotensin level (43.6±11.0 pg/ml) than the eight schizophrenic men (57.6±9.3 pg/ml) (Mann-Whitney z=2.31, p=0.02).

Nineteen of the 20 psychotic patients underwent systematic drug trials with lithium, followed by haloperidol for those who did not respond to lithium, as reported previously (20). Seventeen of the patients responded to drug treatment and could be classified as lithium responders, rapid neuroleptic responders, or delayed neuroleptic responders. Six of the patients either responded to lithium or responded within the first 7 days of subsequent haloperidol treatment. Eleven of the patients had a delayed response to haloperidol after failure to respond to lithium (20).

As we have noted, low CSF neurotensin values appeared primarily among the female psychotic patients. Among these patients, a particular drug response pattern—delayed response to neuroleptic—appeared to discriminate the women whose baseline neurotensin levels were below the 40th percentile of the patients and more than one standard deviation below the mean of the comparison subjects from the women with higher neurotensin levels. The six women who had a delayed response to neuroleptic (requiring 11–35 days to reach a 55% improvement in psychotic symptoms) had a mean±SD baseline neurotensin level of 39.5±8.0 pg/ml, while the four women with other response patterns (to lithium or, subsequently, within the first 5 days, to haloperidol) had a baseline neurotensin level of 58.4±6.0 pg/ml ($t=4.02$, $df=8$, $p=0.002$) (figure 1). No such differences in drug response were found in the male patients; the five men with a delayed response to neuroleptic had a baseline neurotensin level of 60.5±10.1 pg/ml, while the male lithium responder and the male rapid neuroleptic responder had a level of 58.4±22.7 pg/ml ($t=0.19$, $df=5$, n.s.).

The three patients with mood-incongruent affective disorders (two female and one male) had baseline CSF neurotensin levels of 66.0, 57.0, and 42.3 pg/ml, respectively. Neither of the women had responded to lithium, but they responded within the first 4 days to the subsequent neuroleptic trial (rapid responders); the male patient responded to lithium and therefore did not receive a neuroleptic trial. One of the two patients with schizophreniform disorder, a man with a baseline neurotensin level of 74.4 pg/ml, also responded to lithium; the female patient (42.5 pg/ml) failed to respond to lithium but responded to a neuroleptic after the 16th day of treatment (delayed responder).

Baseline, drug-free CSF HVA levels were available for 14 of the 20 patients and for the six comparison subjects. The HVA concentrations ranged from 51 to 171 pmol/ml (mean±SD=100.4±36.8) in the mood-incongruent psychotic patients and from 99 to 322 pmol/ml (192.0±74.7) in the comparison subjects ($t=3.74$, $df=18$, $p=0.002$). The men who were delayed responders ($N=4$) had a baseline HVA level of 94.8±38.8 pmol/ml; the female delayed responders ($N=5$) had an HVA level of 86.0±17.8 pmol/ml ($t=0.45$, $df=7$, $p=0.30$). The remainder of the patients ($N=5$) had a CSF HVA level of 119.4±46.9 pmol/ml.

For the total group of psychotic patients, HVA and neurotensin levels were poorly correlated ($r=0.32$, $df=12$, $p>0.10$). For the delayed responders there was a slight trend toward a positive correlation in the four men ($r=0.85$, $df=2$, $p<0.15$) but not in the five women ($r=-0.52$, $df=3$, n.s.).

Finally, of the four patients who underwent a second lumbar puncture, the patient with a schizophreniform disorder had already fully responded to lithium at the time of the second sampling (day 14 of lithium treatment). He evidenced a small decrease in neurotensin concentration from baseline (74.4 pg/ml) to day 14 of treatment with lithium alone (68.3 pg/ml). In contrast, the three schizophrenic patients who failed to respond to lithium underwent the repeat CSF examination before they had shown a 55% response to haloperidol. One of these neuroleptic-treated patients, reexamined on day 7 of haloperidol treatment, had a 68% increase in neurotensin (from 24.6 pg/ml to 41.4 pg/ml) at the time of the second tap, although she had only a 5% reduction (from baseline) of her psychosis scores; she did not have a 55% reduction from her baseline psychosis scores until day 18 of haloperidol treatment. A second neuroleptic-treated patient had a repeat CSF sampling on day 13 of haloperidol treatment, at which time she showed a 48% reduction of psychotic symptoms; 2 days later she met the 55% criterion for antipsychotic response. Her increase in neurotensin level from baseline was modest (from 44.7 pg/ml to 49.6 pg/ml, or 11%). The third patient who consented to a second lumbar puncture while being treated with haloperidol never responded to haloperidol (or to lithium). This male patient showed an increase in neurotensin level on day 14 after initiation of haloperidol (from 46.6 pg/ml at baseline to 64.7 pg/ml, or 39%), at which time there was but a 5% improvement. In summary, all three patients who were treated with haloperidol and had second lumbar punctures showed a haloperidol-associated increase in neurotensin (mean±SD increase=39.3%±28.5%) that was not positively correlated with clinical status but appeared to precede response in the two patients who subsequently showed a 55% or greater response. In contrast, no such increase in neurotensin occurred in the patient with schizophreniform disorder after successful treatment with lithium.

DISCUSSION

Prompted by a myriad of preclinical studies that have used multidisciplinary approaches to demonstrate interactions of neurotensin with CNS dopamine systems (4–7, 11) and antipsychotic-like effects of this peptide in animals (8–10, 12), we previously documented reductions in CSF neurotensin concentrations in drug-free schizophrenic patients (13–15). In the present study we sought to determine the clinical characteristics of psychotic patients with low neurotensin concentrations. In keeping with our previous results, neither age nor duration of illness was correlated with neurotensin concentration. Our data suggest that a low level of neurotensin may be associated with a delayed but significant response to treatment with an antipsychotic drug. The data also support previous observations that the decrement in neurotensin may be limited to female patients with such a pattern of drug response. Moreover, the psychotic patients who had low neurotensin concentrations (below the 40th percentile for psychotic patients) exhibited more hallucinations, delusions, thought disorder, and behavioral disorganization than did the other psychotic patients. In all three patients who underwent a second lumbar puncture soon after initiation of haloperidol treatment, increases in neurotensin were observed before the major clinical antipsychotic effects. Such an increase in neurotensin had been observed previously (13), and this phenomenon in humans may represent the homologue of the well-documented increase in neurotensin concentration observed in the nucleus accumbens and caudate nucleus of rodents after antipsychotic drug treatment (21), an effect which persists up to 8 months (22).

These findings have important implications. First, they add further evidence of diminished availability of neurotensin in some drug-free schizophrenic patients. Second, they suggest that neuroleptic drugs such as haloperidol increase CSF neurotensin. Third, they also suggest that lipophilic neurotensin agonists which readily cross the blood-brain barrier need to be developed. Such a potentially novel class of antipsychotic compounds may be particularly desirable because of their lack of effects on nigrostriatal dopamine neurons that are believed to produce extrapyramidal side effects and tardive dyskinesia.

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Outcome of Involuntary Medication in a State Hospital System

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Objective: The purpose of the study was to examine the course of involuntarily administered medication in a state hospital population. Method: The authors retrospectively examined the records of all 51 involuntarily medicated patients in six state hospitals in New York City in a single calendar year. Clinical course was recorded for the period of involuntary medication and for 12 months thereafter. These patients were compared to 51 patients on the same wards who accepted medication. Results: Clinicians assessed involuntarily medicated patients as more dangerous to themselves or others and less delusional after treatment than the comparison patients. Long-acting intramuscular antipsychotics were prescribed more frequently for involuntarily medicated patients. No differences were observed in rates of discharge, outpatient cooperation, or rehospitalization. Half of the patients in both groups remained continuously institutionalized, and of those who left the hospital, only 30% of the involuntarily medicated group and 40% of the comparison group took medication as outpatients. Conclusions: For these chronically severely ill patients, involuntary medication did not appear to enhance insight or cooperation or result in rapid return to the community. Involuntary medication is often a necessary short-term, in-hospital management strategy, but it does not replace the need to develop comprehensive, long-term inpatient and community-based approaches to the management of treatment refusal.

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Although the right of committed patients to refuse medication has now been asserted for a decade (1), we know little about what happens after a course of involuntary treatment (2). The rationale for involuntary medication is that it is in the best interest of the patient, will improve the patient's contact with reality and diminish dangerousness to self and others, will help the patient acknowledge the need for continued treatment, and will ultimately yield better treatment compliance. Most studies of involuntary medication focus on patients' reasons for refusing medication. Refusal may be based on the patient's illness, such as psychotic ideas about medication or denial of illness (2–7); legitimate complaints about the treatment itself, including severe side effects or lack of efficacy (3, 8); or the patient's personality, such as the desire to maintain control (2, 5). However, studies have not examined whether our assumptions about the long-term effects of involuntary medication are valid.

While involuntarily medicated patients may later express positive feelings about their treatment (6, 9), the frequency with which such patients continue to take medication after discharge is not known. Previous outcome studies have been rare and long-term follow-up has been neglected. In a small-scale study involving 10 state hospital patients, patients who refused medication remained hospitalized longer and were rehospitalized sooner than those who consented (5). Medication compliance after discharge did not appear to differ from that of matched control subjects.

Most of the landmark legal decisions about involuntary treatment grew out of cases in state hospitals (1, 10). For this reason it is important to study the outcome of involuntary medication among patients in this setting.

This retrospective study examined the inpatient and outpatient histories of a group of state hospital patients who had completed a course of involuntary medication and compared their outcomes to those of a group of matched patients who complied with medication in the hospital. We sought to determine whether involuntarily medicated patients would be 1) less likely to leave the hospital within the study period or have

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TABLE 1. Demographic and Clinical Characteristics of Involuntarily Medicated and Comparison Patients

	Index Patients (N=51)		Comparison Patients (N=51)	
Item	N	%	N	%
Sex				
Men	31	60.8	31	60.8
Women	20	39.2	20	39.2
Ethnic group				
Black	22	43.1	26	51.0
White	22	43.1	15	29.4
Hispanic	6	11.8	10	19.6
Asian	1	2.0	0	0.0
Graduated from high school	26	51.0	23	45.1
Never married	30	58.8	25	49.0
Admission diagnosis				
Schizophrenia	36	70.6	26	51.0
Schizoaffective disorder	2	3.9	5	9.8
Affective disorder	2	3.9	3	5.9
Organic disorder or dementia	2	3.9	2	3.9
Other psychiatric disorder	9	17.6	14	27.5
Unknown	0	0.0	1	2.0
Psychotic symptoms reported on admission				
Thought disorder	4	7.9	7	13.8
Hallucinations	8	15.7	11	21.6
Delusions	25	49.0	21	41.2
Primary clinical indication for treatment				
Dangerous to self or others[a]	45	88.2	37	72.5
Inadequate self-care, regressed	18	35.3	24	47.1
Dangerous to others	15	29.4	11	21.6
Worsening medical condition because of inability to care for self	10	19.6	1	2.0
Suicidal	2	3.9	1	2.0
Severe mental illness, not dangerous	6	11.8	14	27.5

[a] Significant difference between groups ($\chi^2=4.00$, df=1, $p<0.001$).

significantly longer lengths of stay in the hospital, 2) more likely to refuse other inpatient care such as food, personal hygiene, and medical treatment in addition to psychiatric medication, 3) less likely to comply with outpatient treatment after discharge, and 4) more likely to be rehospitalized during the follow-up period.

METHOD

We examined the treatment histories of patients involuntarily hospitalized and medicated in the six state hospitals for adults in New York City, comprising approximately 4,300 beds. Inpatient and outpatient records of all 51 patients who received administrative approval for involuntary medication during the 12-month period from Jan. 1 to Dec. 31, 1985, were reviewed. Fifty-one patients matched for hospital ward and legal status at the time of the index patients' first clinical evaluation for involuntary medication were selected as a comparison group. Ward was selected as a matching variable in order to control for effects of staff attitudes toward the use of involuntary medication. Legal status was selected to control for severity of illness, since the literature indicates that involuntary patients may be more severely ill than voluntary patients (11–13). Records from admission through the 12 months after termination of the index patients' involuntary treatment approval period were reviewed for both patient groups. At the time of the first evaluation for involuntary medication, 40 (78.4%) of the index patients had civil commitment status, six (11.8%) had criminal commitment status, and five (9.8%) were voluntary. Matched patients had identical legal status at the time of the first evaluation. However, the few voluntary index patients were converted to involuntary status, as required by New York State regulations, before the final involuntary medication approval was given.

Legal status on admission was only slightly different in the two groups. Thirty-seven (72.5%) involuntarily medicated patients had civil commitment status, and 10 (19.6%) had criminal commitment status; only four (7.8%) were voluntarily admitted. Among the comparison group, 35 (68.6%) had civil commitment status, six (11.8%) had criminal status, and seven (13.7%) were voluntarily admitted. Three (5.9%) of the matched patients had unknown legal status on admission. Thus, to the extent that involuntary admission correlates with greater severity of illness, the two patient groups were not significantly different on admission.

Data were collected by reviewing all documents generated by the involuntary treatment procedure, including clinical evaluations and final outcome reports, and patients' charts. For the comparison group, all data were obtained from patients' charts. In-hospital medication compliance was measured by reviewing nursing records, which documented the medications ordered and the frequency with which patients accepted them. Outpatient compliance was determined by review of outpatient charts. All inpatient data were derived from New York State hospital records. Chart reviews were supplemented with data from the State Office of Mental Health's computerized patient information system.

The fourth and final judgment regarding involuntary medication for all state hospital patients in New York City in 1985 was made by a physician under the clinical administrative review procedure used at that time in New York State. The review procedure and subsequent changes have been described elsewhere (14).

RESULTS

Fifty-two applications for involuntary medication were made during 1985. This represents 0.37% of the total number of patients in treatment in New York City's adult state hospitals during the 1-year period. One patient's objection to involuntary medication was

TABLE 2. Inpatient Medication and Compliance of Involuntarily Medicated and Comparison Patients

	Total (N=102)		Index Patients (N=51)		Comparison Patients (N=51)		Chi-Square Analysis		
Item	N	%	N	%	N	%	χ^2	df	p
Inpatient antipsychotic medications (N=68)							17.18	1	<0.0001
Intramuscular depot antipsychotic	28	27.5	24	47.1	4	7.9			
Oral antipsychotic	40	39.2	14	27.5	26	51.0			
Inpatient medication noncompliance									
3 months before index patient's involuntary medication (N=92)							35.12	2	<0.0001
>90%	24	23.5	23	45.1	1	2.0			
Intermittent	15	14.7	11	21.6	4	7.8			
<10%	53	52.0	14	27.5	39	76.5			
Period for which index patient's involuntary treatment was approved (N=87)							18.00[a]	2	0.0001
>90%	8	7.8	7	13.7	1	2.0			
Intermittent	19	18.6	17	33.3	2	3.9			
<10%	60	58.8	24	47.1	36	70.6			
Hospitalization within the 12 months after end of index patient's treatment approval period (N=76)							14.29[a]	2	0.0008
>90%	7	6.9	7	13.7	0	0.0			
Intermittent	12	11.8	10	19.6	2	3.9			
<10%	57	55.9	23	45.1	34	66.7			
Noncompliance with other inpatient care									
Refused bathing/other self-care (N=101)	37	36.3	19	37.3	18	35.3	0.02	1	0.90
Refused to eat (N=101)	24	23.5	16	31.4	8	15.7	3.29	1	0.07
Refused medical evaluation/treatment (N=100)	47	46.1	30	58.8	17	33.3	5.84	1	0.02
Improvement in delusions with antipsychotics (N=32)							2.34[a]	1	0.13
Intramuscular depot antipsychotic	17	16.7	16	31.4	1	2.0			
Oral antipsychotic	15	14.7	10	19.6	5	9.8			

[a] Yates' correction for continuity.

upheld. Thus, 51 patients (98%) received administrative approval for involuntary medication. Thirty (58.8%) patients received approval for 3 months, nine (17.6%) for 6 months, five (9.8%) for 9 months, four (7.8%) for 12 months, and three (5.9%) for more than 1 year.

The 51 matched patients were compared with the 51 patients who were involuntarily medicated. The patient groups were not significantly different on any demographic variable. The mean±SD ages of the index and comparison groups were 46.5±15.7 and 44.5±16.0 years. Furthermore, the clinical profiles of the index and comparison groups were similar in terms of known admission diagnosis, psychotic symptoms, and number of previous total (5.0±4.7 versus 5.1±5.1) and involuntary (2.0±2.1 versus 2.5±4.6) psychiatric hospitalizations. However, involuntarily medicated patients were more frequently reported by clinicians as being dangerous to themselves or others than were the matched patients (table 1).

Not surprisingly, despite similar diagnoses, the patient groups differed significantly in the frequency with which they were given depot intramuscular versus oral antipsychotic medication (table 2).

Although intermittent medication refusal was observed in both groups, persistent refusal, as expected, was significantly more common among the involuntarily medicated group than the comparison group. Persistent refusal was defined as a rate of more than 90% noncompliance with prescribed medications in a given period.

Although differences on other measures of compliance failed to reach significance, there appeared to be a tendency among patients who refused medication to be more reluctant to accept other forms of patient care, particularly food. No differences were observed in the number of occasions of restraint or seclusion.

Of the four involuntarily medicated patients with documented thought disorder on admission, two showed improvement in that symptom at the end of the involuntary medication period. Of the seven matched patients with documented thought disorder, two were reported improved. Of the eight involuntarily medicated patients with documented hallucinations, five had improvement in that symptom, while five of the 11 matched patients with documented hallucinations on admission were reported improved. These differences were not statistically significant. Of the 25 involuntarily medicated patients with documented delusions on admission, 15 (60.0%) were less delusional, while only five (23.8%) of the 21 matched patients with documented delusions on admission were reported improved. This difference was statistically significant ($\chi^2=6.09$, df=1, $p<0.02$). This difference was not explained by intramuscular versus oral antipsychotic medication.

TABLE 3. 12-Month Outcome of Involuntarily Medicated and Comparison Patients

	All Subjects				Rehospitalized Subjects			
	Index (N=51)		Comparison (N=51)		Index (N=7)		Comparison (N=8)	
Outcome	N	%	N	%	N	%	N	%
Continuously institutionalized	24	47.1	27	52.9				
Hospital	21	41.2	23	45.1				
Nursing home	3	5.9	4	7.9				
Died because of medical illness while inpatient	2	3.9	0	0.0	0	0.0	0	0.0
Discharged, follow-up available	23	45.1	20	39.2	6	85.7	8	100.0
Eloped without outpatient plan	4	7.8	5	9.8	1	14.3	1	12.5
Refused outpatient referral	4	7.8	1	2.0	2	28.6	0	0.0
Refused outpatient referral, died by suicide	1	2.0	0	0.0	0	0.0	0	0.0
Never attended clinic	4	7.8	4	7.8	1	14.3	2	25.0
1 or 2 clinic visits only	2	3.9	2	3.9	1	14.3	1	12.5
Complied with visits but not medication	1	2.0	0	0.0	0	0.0	0	0.0
Complied with visits and medication	7	13.7	8	15.7	1	14.3	4	50.0
Discharged, no follow-up	2	3.9	4	7.8	1	14.3	0	0.0
Outpatient records unavailable	1	2.0	4	7.8	1	14.3	0	0.0
No outpatient medication prescribed; patient to seek substance abuse treatment	1	2.0	0	0.0	0	0.0	0	0.0

The median length of stay for the overall hospital population was 52 days. The involuntary groups we examined had considerably longer stays. Involuntarily medicated patients had a mean±SD hospital stay of 35.7±43.1 months. Matched patients had a mean stay of 66.5±123.8 months. Although there was a large between-group difference, it was not statistically significant because of the large standard deviations.

Table 3 summarizes rates of attendance at outpatient facilities after discharge, medication compliance, and rehospitalization for both patient groups. There were no significant differences in postdischarge outcome between those who were involuntarily medicated and those who accepted medication voluntarily.

After 12 months, approximately one-half (N=24, 47.1%) of the involuntarily medicated patients remained institutionalized. When the two patients for whom follow-up was not relevant or available (one was not prescribed medication, one had no available records) were excluded, only seven (30.4%) of the 23 involuntarily medicated patients who left the hospital complied with clinic visits and accepted medication. After 12 months, 27 (52.9%) of the matched patients were still institutionalized. Of 20 who left the hospital and for whom follow-up was available, only eight (40%) complied with clinic visits and medication.

Rehospitalization rates were derived from the New York State hospital inpatient database and records. Non-state-hospital records could not be obtained. One involuntarily medicated patient was rehospitalized after 9.7 months despite compliance with outpatient medication. Four outpatient, medication-compliant matched patients were rehospitalized after a mean of 11.9±4.6 months. These rates were not statistically significant.

DISCUSSION

The large state hospital system in New York City appears to reserve the use of involuntary medication for the patients who most persistently refuse medication and who are also considered dangerous to themselves or others. Although the median length of stay for all state hospital patients was 52 days, the average patient approved for involuntary medication had already been in the hospital for 17.5 months. Comparison patients also had long stays because they were selected from the same wards as the patients who had refused medication, and, generally speaking, these were units designated for long-term care rather than for newly admitted patients. Patients for whom formal petitions for involuntary medication were made may have exhausted most other treatment options.

This study, then, compared two groups of long-stay involuntary patients: those who refused both hospitalization and medication and those who refused hospitalization but, once institutionalized, complied with medication. Involuntarily medicated patients were reported to be significantly less delusional than matched patients at the end of the involuntary treatment period. This difference was not explained by greater use of depot medications. This benefit must be interpreted with caution. The difference in improvement rates may be biased, since extensions of involuntary medication were granted on the basis of clinicians' progress reports. Furthermore, while delusions were reportedly ameliorated after a course of involuntary medication, improvement had no impact on long-term outcome.

A course of involuntary medication did not appear to have either a negative or a positive effect on long-term outcome. We did not find significant differences in hospital course or outpatient compliance between the two patient groups. Whether or not they complied with in-hospital medication, 60%–70% of patients were resistant to continuing treatment after discharge.

This study could have underestimated treatment compliance, since patients who left the hospital without consent and never reentered the state system may have sought treatment elsewhere. However, it is more likely that the number of patients discontinuing treatment is an underestimate, since outpatient medication compliance records were based on patient self-reports. Our results are consistent with previous findings of a long-term unwillingness among committed patients to engage in follow-up services (12). Patients' resistance was also reflected in refusal of food, self-care of personal hygiene, and medical treatment while in the hospital, which occurred among patients who accepted psychotropic medication as well as those who rejected it.

Involuntarily medicated patients were more likely to persistently refuse medication as inpatients and to receive treatment with long-acting, intramuscular antipsychotic drugs. Psychiatrists appear to prescribe long-acting antipsychotics to avoid continuous confrontation between the patient and the nursing staff or to ensure that the patient does not evade the medication in pill form. This desire to be certain that patients receive medication may follow from the apparently dire status of the illness presented to clinicians; 88.2% of involuntarily medicated patients were dangerous to themselves or others. This is consistent with the evidence that of patients who refuse medication, those who reach the formal review process are more severely ill than are those who can eventually be persuaded by clinicians to accept medication and those discharged without receiving a course of medication (15).

With the severely ill population studied, involuntary medication appeared to be a necessary management tool for in-hospital care (14); but for most, it did not result in rapid return to the community or later compliance with medication. For many long-stay chronic patients, a course of involuntary medication in the hospital appears to be a short-term strategy that does not produce the insight and cooperation that psychiatrists hope to achieve.

Although some investigators have found that committed patients later accept voluntary hospitalization (16, 17) and that involuntarily medicated patients later express agreement with the need for treatment (9), those studies were performed in general hospital settings with less chronic patients and did not examine medication compliance. Our study was conducted in state hospitals with a chronic mentally ill population. Among the chronic mentally ill, treatment refusal may be associated with severe illness incompatible with rapid discharge, and even when discharge is possible, may be associated with persistent refusal despite improvement with medication. The patients we studied had numerous previous psychiatric hospitalizations, many of which were involuntary. Medication refusal may reflect a well-entrenched pattern of resistance to treatment. In that case the results of this study suggest that it may be counterproductive to wait to intervene only when refusal is persistent and the patient is chronically ill and that earlier intervention may be more successful. Alternatively, these patients may have a more severe form of illness (15) that might affect their appreciation of the need for treatment even if there is symptom improvement with medication.

Our findings suggest that it may be important to consider alternatives for the long-term management of patients who refuse treatment. When treatment refusal has become a chronic pattern, those in need of continued care could be considered for an expanded use of outpatient commitment (18–20). However, not all patients who refuse treatment are appropriate for aggressive intervention in or out of the hospital, either because they are competent to reject care or can function adequately, if not optimally, even without treatment or because the treatment does not produce sufficiently beneficial therapeutic results. For these patients we need to consider more successful strategies of engagement including provision of sanctuary without treatment in the community. Sanctuary could provide shelter and food while clinicians work to encourage patients to accept mental health services.

While we obtained 12-month follow-up data on 50 (98%) of 51 patients who had completed a course of involuntary medication in a state hospital and on 47 (92%) of 51 matched comparison subjects, this study was retrospective in nature and thus limited in terms of the factors that could be explored and the ability to make causal inferences. We examined only committed patients whose stays were far longer than the typical state hospital patient's. In addition, we did not examine routine refusals that were allowed by staff; our system reserves involuntary medication for chronic, persistent refusal within a population so severely and chronically ill that they may be least likely to respond to the intervention. We urge the prospective examination in both inpatient and outpatient settings of the issues we have described here in order to develop better models for addressing medication refusal among severely mentally ill patients.

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Clinical Features of Cocaine-Induced Paranoia

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Objective: The authors' objective was to assess the frequency and nature of cocaine-induced paranoia. Method: They interviewed 50 cocaine-dependent men consecutively admitted to a 28-day rehabilitation program. Results: Thirty-four (68%) of the 50 men reported highly distressing transient paranoid states in the context of cocaine use. The men who experienced paranoia did not differ from those who did not in age, race, or measures of cocaine use. The mean duration and amount of cocaine use before development of paranoia of the men who reported paranoia were not significantly different from the mean lifetime duration and amount of cocaine used by the men who did not report paranoia. Paranoia became more severe and developed more rapidly with continued cocaine use. Conclusions: The transient paranoid state appears to be a common feature of cocaine dependence and does not seem to be simply a result of exceeding a threshold of use. Rather, affected individuals might possess a predisposition to this drug-induced state. The fact that paranoia became more severe and developed more rapidly with continued drug use is consistent with a sensitization model of cocaine-induced paranoia. In vulnerable individuals, limbic sensitization may underlie its expression, but localization to a specific brain region is speculative. Quantity of use and route of administration do not appear directly to predispose to this phenomenon. Future investigations must be aimed at uncovering the markers and meaning of vulnerability to transient paranoia in heavy cocaine users.

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Induction of paranoid psychoses by amphetamines and other psychomotor stimulants has long been documented (1). However, observations of cocaine-associated paranoid psychoses have been less frequent and systematic (2–5).

Documentation of cocaine psychoses has been limited to extreme cases such as episodes of violence, suicide, murder, and child abuse (6). In a case series of five Bahamian cocaine smokers, Manschreck et al. (7) described florid paranoid symptoms lasting for days or weeks. In a separate chart review (8), these authors estimated that 30% of a Bahamian sample manifested extended paranoid psychoses following cocaine use. However, many of the Bahamian subjects had premorbid psychiatric disorders, so it is not clear whether cocaine had precipitated psychoses in predisposed individuals or psychoses were induced de novo. Importantly, in agreement with other, less systematic reports, these authors found a markedly higher incidence of transient paranoia during binges of cocaine use.

In this paper we define "transient" (or binge-limited) paranoia as a self-limited paranoid experience that is confined to the episode of cocaine use. The paranoia is no longer present when the individual has emerged from post-binge hypersomnolence, or "crash." By contrast, "persisting" paranoia refers to sustained paranoia lasting for days, weeks, or longer after the crash. Although persisting paranoia is typical of functional psychiatric illness, it has rarely been reported in cocaine abusers.

We systematically evaluated cocaine-induced paranoia in a group of 50 cocaine abusers seeking treatment. Using extant and new instruments we evaluated 1) the prevalence of cocaine-induced transient versus persisting paranoia, 2) associated use patterns and patient characteristics, 3) qualitative features of the cocaine paranoid phenomenon, and 4) the clinical and historical features that distinguish individuals who experience cocaine-induced paranoia from those who do not report such experiences.

METHOD

The subjects were 50 consecutive patients admitted for primary cocaine dependence. The first 50 patients

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meeting study criteria (all male) were asked to participate in the study, and all of them accepted. All were patients voluntarily entering an inpatient substance abuse rehabilitation program at a Veterans Administration hospital.

All patients met *DSM-III-R* criteria for cocaine dependence. Individuals who also met *DSM-III-R* criteria for current dependence on any other substance were excluded. Subjects who used another substance were included if their cocaine use was primary (i.e., the other substance or substances were used to modify the acute effect of cocaine and there was no abuse of the substance or substances in the absence of cocaine intoxication).

We excluded patients with *DSM-III-R* axis I psychotic disorders and bipolar illness as well as those with axis II schizoid and schizotypal personalities. No patient reported a history of psychosis in first-degree relatives. Previous psychiatric admissions that related to substance use (e.g., detoxification, acute admission for toxic psychoses, or transient suicidality in the context of alcohol or cocaine intoxication) were permissible. Screening for inclusion was performed by one of us (S.L.S.); patients were interviewed between day 21 and day 28 of their admission.

The mean±SD age of the patients at admission was 34.3±5.8 years. Twenty-three were non-Hispanic white, 23 black, and four Hispanic. All of the patients were in Hollingshead socioeconomic classes 3 and 4. At admission, 10 (20%) of the patients used cocaine intranasally, nine (18%) intravenously, and 31 (62%) by inhalation (free base).

The patients were evaluated in a 30–45-minute session by using a rater-administered 57-item questionnaire (the Cocaine Experience Questionnaire, available on request) that assesses methods and patterns of cocaine use as well as the nature and extent of paranoid experiences associated with use. Cocaine use was assessed twice—first by rater-administered questionnaire (the Cocaine Abuse History and Inventory [9]) and then by chart review. Family history of functional psychotic symptoms was elicited during administration of the Cocaine Experience Questionnaire. All patients provided informed consent before participating in the interview.

The patients were carefully instructed to distinguish adaptive hypervigilance or anxiety when in a high-risk situation (e.g., making drug deals, passing through housing projects, engaging in illicit activity) from completely irrational beliefs (e.g., the police are standing on the ledge of their tenth-floor apartment window).

We used grams as the unit of quantification even though the individual cocaine samples obtained by the patients varied in purity both among and within patients. Fluctuations in cocaine purity do not invalidate the gram as a meaningful measure because differences in purity should randomize among and within these patients, all of whom obtained cocaine in the same geographic region and had similar socioeconomic backgrounds. Fluctuation of purity should actually contribute to the error variance and the likelihood of committing a type II error.

Patient-reported duration of use was measured from the time of first regular use (i.e., weekly use for at least 2 months) until admission. Although the accuracy of such retrospective data cannot be definitively established, inaccuracy should also be randomly distributed and contribute to the error variance. In some cases, patients had used cocaine for more than 5 years. Time spent abstinent due to incarceration or previous substance abuse treatments was deducted from the number of months of total use. Although the accuracy of such retrospective data cannot be definitively established, inaccuracy should also be randomly distributed and contribute to the error variance. Lifetime consumption exceeding 4 kg was truncated to 4 kg in particular analyses.

Patients who developed cocaine-induced paranoia were compared with those who did not on demographic and drug use variables. Data were analyzed with t tests and chi-square tests. We used one-tailed tests in many of the analyses because of the unidirectional nature of the hypothesis; namely, we expected that the paranoid group would have a more severe drug use history.

RESULTS

Black and Hispanic patients (N=27) did not differ from white patients (N=23) in age at first use of cocaine, amount of lifetime exposure, duration of use, or the probability of developing paranoia. The nonwhite patients who developed paranoia did not differ from the white patients who did so in the time to the onset of paranoia after beginning regular use.

The Paranoid Experience

Thirty-four (68%) of the 50 patients developed transient paranoid episodes during cocaine use; these are different from the prolonged paranoid episodes that have been described in amphetamine abusers. All of the patients who experienced paranoia used cocaine in binges (periods of sustained use lasting between 8 and 72 hours). The paranoia of all but one of the patients had resolved by the time he woke from the crash. This one patient had a paranoid experience that extended 6–8 hours after the crash.

Typical paranoid ideation included the suspicion or belief that the police or drug dealers were about to apprehend him or that others in the room were planning to attack him and steal cocaine. Frequently, actual stimuli (sounds and flashes of light) were misinterpreted as evidence that menacing individuals were immediately outside the room or window preparing to enter. All of the paranoid patients found these experiences distressing and, not infrequently, terrifying. None described perceptual hallucinations or bizarre delusions.

Eighteen (53%) of the 34 paranoid men acted on their paranoid ideations by checking activities (relocking doors, scanning out of windows), hiding in closets or under the bed, or refusing to leave a contained place such as a car. Thirteen (38%) of the paranoid patients actually armed themselves with a gun or knife for protection (two used these weapons, fortunately without tragic results). Twenty-three (68%) felt less paranoid when they used cocaine by themselves, and 30 (88%) reported that they felt much safer when they used it in familiar settings.

Twenty-six (76%) of the 34 patients reported that their paranoid experiences worsened with continued cocaine use; none claimed that the paranoia lessened over time. This was true even for the three patients who decreased the rate (in grams/week) of their cocaine consumption after the onset of paranoia. Twenty (59%) of the men also described a more rapid onset of paranoia (from 15–90 minutes to 5–10 minutes after ingestion) over the course of cocaine use.

The 34 patients also claimed that paranoid ideation lasted for hours—far exceeding the amount of time they would experience the pleasurable cocaine high (estimated to be minutes). Some described an early superimposition of the high by paranoid ideation that did not dissipate until long after the high was gone. (All 50 patients claimed that the cocaine high itself had decreased in intensity and pleasurable quality from the onset of regular use until the time of admission.)

Thirteen (38%) of the patients who developed paranoia deliberately attempted to "medicate" their paranoia with alcohol and/or opiates. On a 6-point ordinal scale ranging from 1=neutral to 6=intolerable, there was a trend for these 13 patients to report greater distress associated with paranoia than did those who did not try to so medicate themselves ($t=1.7$, $df=32$, $p<0.10$). This heightened negative experience, in fact, may have led to their self-medicating efforts. In no instances did these 13 patients report complete suppression or prophylaxis of paranoia with opiates or alcohol; rather, they experienced a reduction in the intensity of the experience.

There was a considerable range of duration of cocaine use before the onset of paranoia. Specifically, 17 (50%) of the 34 patients experienced the onset of paranoia within 25 months after beginning regular use. An additional 12 patients first became paranoid between 25 and 57 months after beginning regular use. The remaining five patients developed paranoia after 57 months of use. Although most of the patients first developed paranoia well before the index admission, three of the 34 patients first experienced paranoia within the month before admission.

The general longitudinal pattern of cocaine use was comparable in patients who did and did not experience cocaine-induced paranoia. Irrespective of actual duration of use, the dominant trend since beginning regular use was a plateau culminating in a rise in consumption within the year before admission. In all but three of the paranoid patients, cocaine use was sustained at the before-paranoia level for at least 12 months after the onset of paranoia.

Comparison of Paranoid and Nonparanoid Patients

The 34 paranoid and 16 nonparanoid patients did not differ from each other with respect to age, race, or route of cocaine administration at admission.

The paranoid patients described the onset of binge-limited paranoia after a mean duration of 34.7±31.5 months of use. Although this period of time tended to be shorter than the lifetime duration of use by nonparanoid patients (50±50 months), the difference was not significant. Similarly, although the quantity of cocaine to which the paranoid patients were exposed until the onset of paranoia tended to be less than the lifetime quantity to which nonparanoid patients were exposed (0.82±1.8 kg versus 1.34±1.7 kg), the difference was not significant.

The two groups of patients did not differ in concurrent use of other drugs such as alcohol, cannabis, opiates, benzodiazepines, and amphetamine. More of the paranoid than the nonparanoid patients reported remote past use of hallucinogens (15 [44%] versus three [19%]) ($\chi^2=3.23$, $df=1$, $p<0.07$), but use of other drugs and alcohol did not differ between groups. No patient reported paranoia when using alcohol or opiates in the absence of cocaine. Those patients in both groups who reported cannabis-related paranoia explicitly denied using marijuana in direct combination with cocaine.

DISCUSSION

The major findings of this descriptive study are 1) cocaine-induced, binge-limited paranoia was prevalent in a sample of heavy users, 2) such paranoia did not appear to be associated with quantitative measures of cocaine use (e.g., duration and amount), 3) despite the development of paranoia, affected patients continued to use cocaine at the same rate, and 4) cocaine-induced paranoia became both more intense and was manifested earlier in the course of the cocaine binge as use continued.

Transient or binge paranoia during episodes of cocaine use was found in 68% of 50 patients. Persisting paranoia occurred for a brief period in only one patient. This appears to differ from accounts of amphetamine abuse in which the development of persisting paranoia is more common (1, 5). It remains possible, although not demonstrated by our data, that transient paranoia may develop into persisting paranoia if cocaine abuse continues; prospective follow-up data will be needed to assess this.

The observation that patients who developed paranoia did so after comparable durations and amounts of exposure to cocaine as the nonparanoid group strongly suggests that the development of paranoia is not simply a result of surpassing a threshold of use. It implies that affected individuals are predisposed to this drug-induced state. One potential predisposing factor, previous substance abuse other than cocaine, showed that the paranoid patients were more likely to have used hallucinogens before becoming dependent on cocaine. Although toxic actions or interactions of other agents such as hallucinogens could produce paranoia, it is also possible that other drug use acts only as an independent marker (i.e., it may appeal more to individuals prone to paranoia). Other potential yet unexplored vulnerability factors for the development of cocaine-induced paranoia may reside in family history, individual personality traits, or individual neurophysiological features.

The observation that patients found cocaine paranoia nearly intolerable but did not decrease their rate or frequency of cocaine use in the face of an intensely aversive consequence reflects the intense positive reinforcing properties of cocaine. It is likely, of course, that individuals who discontinued or diminished their consumption in response to the development of paranoia would be missed by our study. They represent an intriguing but less accessible future comparison group.

An inverse relationship was noted between the cocaine high and paranoia. The high was reported to be less pleasurable but the intensity of paranoid experiences increased with continued use. This suggests that the mechanisms producing paranoid ideation are different from those mediating the reinforcing aspect of the addiction.

Preclinical studies have clearly established that cocaine and related agents, such as lidocaine and procaine, pharmacologically induce sensitization: abnormal neuronal sensitivity has been demonstrated in the limbic area (10, 11). This same region has been implicated in toxic affective and psychotic reactions as well as panic attacks, mania, depression, and visual hallucinations (12–15). Theoreticians have predicted stimulant-induced paranoia (16, 17) on the basis of animal models of kindling and sensitization. Our data may be partially supportive of such a model of cocaine-induced paranoia. Clinically, our patients described an increasing rapidity of onset of paranoia during binges, typically progressing from about an hour to within minutes of initiating the binge. Thus, diminished neuropharmacological stimulation (cocaine "inoculation") produces an equivalent or greater response (paranoia). It is possible that conditioned expectation of paranoia played a role in its augmentation over time.

This report is limited by a partially retrospective design and a small study group, both of which could have led to type II errors. Reliance on grams should have made the variability of responses greater due to questionable accuracy of recall and fluctuations in drug purity. Only systematic differences in reporting between the paranoid and nonparanoid patients might invalidate the findings, and no such differences were observed. Within the paranoid group, descriptions of the paranoid experience and ratings of severity are prone to distortions that can accompany not only self-reports but recollections of time-limited states of altered perception.

In conclusion, the transient paranoid state appears to be a common feature of cocaine dependence. In vulnerable individuals, limbic sensitization may underlie its expression, but the localization of paranoid phenomena to a specific brain region is speculative at this time. Quantity of use and route of administration do not appear directly to predispose to this phenomenon. Future investigations must be aimed at uncovering the markers and meaning of this vulnerability to transient paranoia in heavy cocaine users.

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Lymphocyte Glucocorticoid Receptor Number in Posttraumatic Stress Disorder

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Objective: The authors' objective was to investigate the possibility that glucocorticoid receptor changes may be involved in the dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis in posttraumatic stress disorder (PTSD). Method: They measured the number of lymphocyte cytosolic glucocorticoid receptors and plasma cortisol concentrations in 15 consecutively admitted male combat Vietnam veterans with PTSD and in a normal comparison group of 11 subjects. Results: Both the patients and the normal comparison subjects showed a morning-to-afternoon decline in glucocorticoid receptor concentrations, paralleling the normal diurnal decline in cortisol levels. The number of glucocorticoid receptors was 63% greater in the morning and 26% greater in the afternoon in the patients with PTSD than in the normal subjects. No group differences in cortisol levels were observed, nor were glucocorticoid receptor number and cortisol levels correlated. The number of morning glucocorticoid receptors was positively correlated with symptoms of PTSD and anxiety. Conclusions: These results provide further evidence for a dysregulation of the HPA axis in PTSD. The finding that patients with PTSD had a substantially greater number of lymphocyte glucocorticoid receptors than normal comparison subjects is consistent with the authors' previous observations of low 24-hour urinary cortisol excretion in subjects with PTSD. Furthermore, the receptor changes observed are opposite of those reported in major depressive disorder. The present data, along with other findings of HPA abnormalities in PTSD, support the possibility of a greater negative feedback sensitivity at one or more levels of the HPA axis.

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Although stress is a major etiologic factor in posttraumatic stress disorder (PTSD), there have been surprisingly few investigations of the hypothalamic-pituitary-adrenal (HPA) axis in this disorder. Despite the paucity of studies, however, there is emerging evidence for HPA dysfunction in chronic PTSD. Moreover, the biological data seem to distinguish PTSD from other psychiatric disorders such as major depressive disorder.

Previous work in our laboratory has shown that patients with PTSD have lower urinary-free cortisol levels than patients with major depressive disorder (1) and normal comparison subjects (2). Consistent with these data, the cortisol response to the standard 1-mg dose of dexamethasone has been found to be either within the normal range (3, 4) or exaggerated (5) in PTSD. In contrast, major depression has been associated with hypercortisolemia, which in a subgroup of patients is reflected in nonsuppression of cortisol in response to dexamethasone (6).

There is also evidence for a blunted ACTH response to corticotropin-releasing factor (CRF) in patients with PTSD (7). A blunted ACTH response to CRF has also been observed in major depressive disorder; however, the mechanisms underlying this response are likely to be different in the two disorders. In PTSD, the attenuated ACTH response occurred in the presence of normal afternoon plasma cortisol levels (7). In contrast, in major depressive disorder a blunted ACTH response occurs with hypercortisolemia, possibly reflecting a lower number of pituitary CRF receptors caused by hypothalamic CRF hypersecretion (8, 9) and/or an altered negative feedback inhibition of the pituitary (10).

In the aggregate, the findings of low cortisol excretion and blunted ACTH responses to CRF in chronic

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TABLE 1. Age and Clinical Information for 15 Patients With PTSD

Subject	Age (years)	Medications	Comorbid RDC Diagnosis	Hamilton Anxiety Score	Hamilton Depression Score	Mississippi PTSD Score
1	41	Buspirone	Substance abuse	27	22	147
2	37	Diazepam, imipramine, perphenazine	Major depressive disorder	38	35	191
3	42	Desipramine	None	11	9	123
4	37	Tranylcypromine	Substance abuse	21	23	144
5	39	Clonidine	Substance abuse	16	15	132
6	39	Imipramine	Panic disorder	28	28	136
7	39	Lorazepam, diphenhydramine	Major depressive disorder	20	33	129
8	39	Temazepam, desipramine, propranolol	None	34	24	137
9	39	Clonidine	None	24	24	112
10	39	None	Substance abuse	20	22	115
11	39	None	Major depressive disorder	15	16	107
12	42	None	Substance abuse	14	19	117
13	40	None	None	17	22	122
14	37	None	Major depressive disorder	17	32	112
15	45	None	Major depressive disorder	19	24	137

PTSD suggest a disturbance in adrenocortical regulation, which may be due to alterations in tissue sensitivity and/or negative feedback at one or more levels of the HPA axis, perhaps secondary to changes in hormone receptor sensitivity. Because circulating corticosteroid concentrations have been found to produce dynamic changes in the number of glucocorticoid receptors in a variety of target tissues in the brain (11, 12) and lymphocytes (13), the lower cortisol levels observed in chronic PTSD may be associated with an increased number of glucocorticoid receptors in neurons and/or lymphocytes.

An altered negative feedback sensitivity within the HPA axis has also been postulated in major depressive disorder. In this case, feedback sensitivity is reported to be less, paralleling the lower number of glucocorticoid receptors in lymphocytes (14, 15). To further investigate the possibility that glucocorticoid receptor changes may be involved in the dysregulation of the HPA axis in PTSD, we measured morning and afternoon plasma cortisol concentrations and the number of glucocorticoid receptors in circulating lymphocytes in patients with chronic PTSD and in a normal comparison group.

METHOD

Fifteen consecutively admitted male Vietnam combat veterans (age range=37–45 years, mean±SD=39.5±2.1, median=40) with a primary diagnosis of PTSD and 11 healthy men (age range=30–56 years, mean=37.8±7.48, median=37) participated in the study after giving voluntary, written informed consent. PTSD was diagnosed by using the Structured Clinical Interview for DSM-III-R (SCID) (16) and the Mississippi Scale for Combat-Related PTSD (17); a cutoff of 107 was used on the Mississippi scale. Other diagnoses were made according to *DSM-III-R* by consensus from results of structured diagnostic interviews (SCID or the Schedule for Affective Disorders and Schizophrenia) and assessments by the treating psychiatrist and ward chief. Five of the 15 patients had a comorbid diagnosis of major depressive disorder, and five had comorbid substance abuse or dependence. Patients were excluded if they met criteria for a psychotic or organic condition; had substantial medical illness as determined by history, physical examination, and routine laboratory screening; regularly used more than 3 oz of absolute alcohol per day; or had used street drugs within 3 weeks of the drawing of blood. Nine of the 15 patients were being treated with medications, including antidepressants and anxiolytics.

Blood was obtained by venipuncture at 8:00 a.m. and 4:00 p.m., and mononuclear cells were isolated by using Ficoll Hypaque within 1 hour following the drawing of blood. Cells were centrifuged at 300 *g* at 4 °C, washed four times in ice-cold Hank's buffer, and pelleted. An aliquot of the lymphocyte suspension was counted by a Coulter counter, and the final pellet was stored at −70 °C. An aliquot of plasma was also frozen for subsequent determination of cortisol levels.

Clinical ratings were made by two raters (R.Y. and S.M.S.) on the day blood was drawn. Anxiety and depression were assessed by using the Hamilton Rating Scale for Anxiety (18) and the Hamilton Rating Scale for Depression (19). Patients also completed the Mississippi Scale for Combat-Related PTSD (17), which served as both a diagnostic instrument and a measure of severity of combat PTSD.

Combat exposure was rated on a scale of 0–56 by using the expanded Combat Exposure Scale (20). Pa-

TABLE 2. Effect of Comorbidity on Cortisol and Number of Glucocorticoid Receptors in 15 Patients With PTSD[a]

	Number of Glucocorticoid Receptors				Plasma Cortisol Level (μg/dl)			
	Morning		Afternoon		Morning		Afternoon	
Group	Mean	SD	Mean	SD	Mean	SD	Mean	SD
PTSD with major depressive disorder (N=5)	3702	1317	1657	873	16.1	3.1	6.6	1.5
PTSD without major depressive disorder (N=10)	3366	1379	1726	970	12.8	2.8	8.9	3.5
PTSD with substance abuse (N=5)	3004	1050	1760	1356	13.2	3.9	7.6	3.2
PTSD without substance abuse (N=10)	3694	1617	1675	680	15.0	3.4	8.5	3.3

[a]The small number of subjects in this analysis raises the possibility of a type II error.

tients were also interviewed with the Atrocity Scale (21), which quantifies exposure to and/or participation in particularly traumatic combat-related behaviors on a scale of 6–36 (6=no experience of any atrocities and 36=active participation in all).

Binding of glucocorticoid receptors was measured with the highly selective type II glucocorticoid ligand ^{3}H-RU 28362 according to Lowy (22). Briefly, the frozen lymphocyte pellets (containing 50–100×10^6 cells) were suspended in the assay buffer (consisting of 10 mM Tris, 1 mM EDTA, 2.5 mM dithiothreitol, 10% glycerol, 20 mM Na_2MoO_4; pH 7.4), mixed vigorously in the cold for 30 minutes, then spun at 250,000 *g* for 30 minutes. Total binding of ^{3}H-RU 28362 (specific activity=77 Ci/mmol) was measured in 0.25 ml aliquots of cytosol, which were incubated overnight at 4 °C with 10 nM of ligand. Specific binding was defined as that inhibited by a 500-fold excess of unlabeled RU 28362. The 10-nM concentration of ^{3}H-RU 28362 measures 90% of available receptors and correlates highly (r=0.99) with B_{max} values (22).

For the determination of cortisol levels, untreated plasma samples were thawed and cortisol levels analyzed by using a radioimmunoassay kit procedure developed by Clinical Assays, Inc. (Cambridge, Mass.). The interassay coefficient of variation for this method was 4.0%. Binding assays and radioimmunoassays were done blind to the subjects' diagnoses.

Differences between patients with PTSD and normal subjects were assessed with repeated measures (22) two-tailed analysis of variance (ANOVA). Repeated measures ANOVA was also performed to determine the effects of comorbidity of major depressive disorder and substance abuse or dependence and the effects of medication status on biological measures. Clinical data from subgroups of the patients with PTSD were assessed with Student's t test. Post hoc testing was performed with the Tukey test. Correlational analyses were performed with Pearson's r. Group values are expressed as mean±SD.

RESULTS

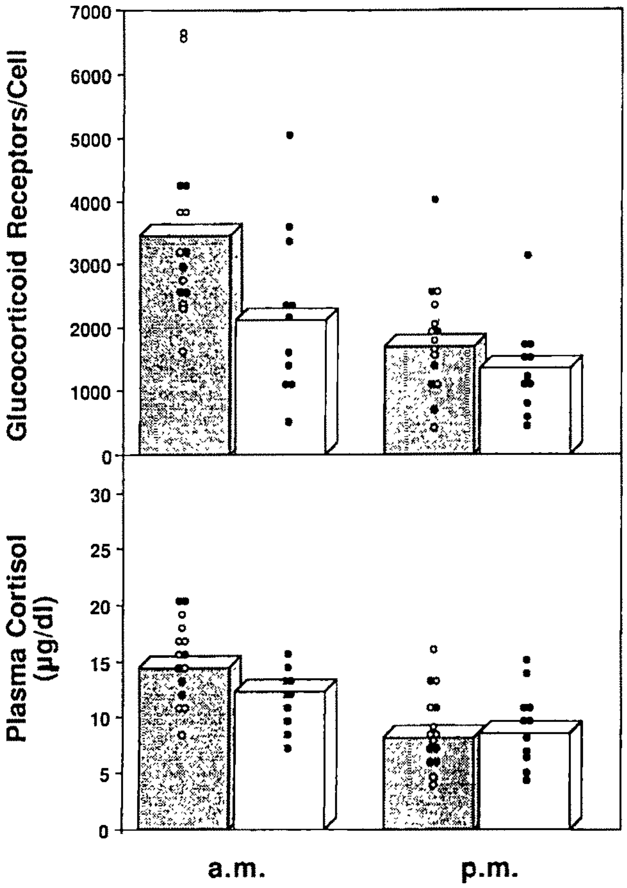
The patients' ages and individual clinical ratings are presented in table 1. Subdividing patients on the basis of presence or absence of major depressive disorder revealed that PTSD patients with comorbid major depressive disorder (N=5) had significantly higher scores than did those without major depressive disorder (N=10) on the Hamilton depression scale (28.0±7.9 versus 20.8±5.3; t=2.10, df=13, p=0.05) but not on the other clinical rating scales. No differences in clinical symptoms were observed between PTSD patients with (N=5) and without (N=10) comorbid substance abuse or dependence. Medicated patients with PTSD (N=9) had significantly higher scores on the Mississippi Scale for Combat-Related PTSD than unmedicated patients (N=6) (139.0±22.2 versus 118.3±10.4; t=2.11, df=13, p=0.05). Medicated patients also tended to have higher Hamilton anxiety scale scores (24.3±8.5 versus 17.0±2.3; t=2.04, df=13, p=0.06).

As a group, the 15 patients with PTSD had a significantly greater number of glucocorticoid receptors than the 11 normal comparison subjects (F=4.79, df=1, 24, p<0.05). This difference was greater in the morning (63% higher; p<0.05) than in the afternoon (26% higher, n.s.). There were no group differences in morning or afternoon plasma cortisol concentrations. There were overall diurnal changes in the number of glucocorticoid receptors and cortisol concentrations: both measures were significantly higher in the morning than in the afternoon (F=30.09, df=1, 24, p<0.0001; figure 1). There was also a trend for a Group by Time interaction in the number of glucocorticoid receptors (F=3.94, df=1, 24, p=0.06), indicating a steeper morning-to-afternoon decline in the number of glucocorticoid receptors in the patients with PTSD. There were no significant differences in biological variables when the patients with PTSD were subdivided on the basis of medication status (figure 1).

No biological differences as a result of comorbidity were found in patients with PTSD (table 2). Therefore, data from all patients were combined for the purpose of correlational analysis.

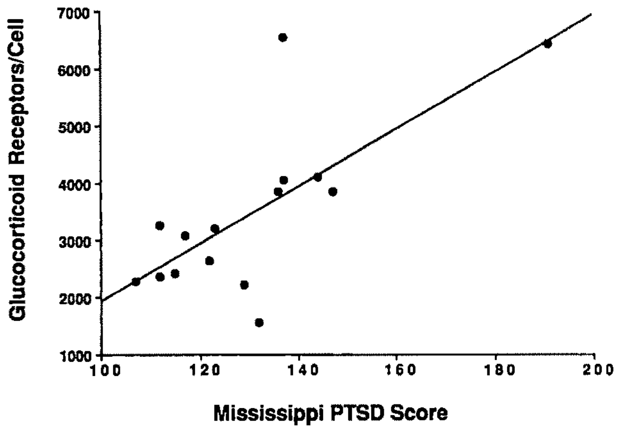
The morning and afternoon numbers of glucocorticoid receptors were positively correlated in the patients with PTSD (r=0.498, df=13, p<0.05) and in all subjects combined (r=0.517, df=24, p<0.05). Comparison subjects showed a nonsignificant trend toward a relationship between morning cortisol levels and the

FIGURE 1. Cortisol Level and Number of Lymphocyte Glucocorticoid Receptors in 15 Patients With PTSD and 11 Comparison Subjects[a]



[a]The shaded blocks are patients with PTSD; the unshaded blocks are comparison subjects. Open circles represent medicated patients; closed circles represent unmedicated patients. The morning levels of glucocorticoid receptors in the patients with PTSD were significantly different from those of the comparison subjects (p<0.05, post hoc Tukey test).

FIGURE 2. Relationship Between Number of Glucocorticoid Receptors and PTSD Symptoms Assessed by the Mississippi PTSD Scale[a]



[a]r=0.73, df=14, p<0.005.

morning number of glucocorticoid receptors (r= 0.436, df=10, p=0.18). This trend was absent in the patients with PTSD (r=0.189, df=14, p=0.50).

The morning number of glucocorticoid receptors was significantly correlated with severity of combat-related PTSD symptoms as assessed by the Mississippi scale (figure 2). It was also significantly correlated with anxiety symptoms measured by the Hamilton anxiety scale (r=0.784, df=14, p<0.001). There was a nonsignificant association between the morning number of glucocorticoid receptors and Hamilton depression scale scores (r=0.402, df=14, p<0.10).

Exposure to combat was not related to the morning number of glucocorticoid receptors (r=0.032, df=12, n.s.) but was significantly correlated with morning plasma cortisol concentrations (r=0.489, df=12, p< 0.05). Scores on the Atrocity Scale were significantly correlated with the morning number of glucocorticoid receptors (r=0.554, df=12, p<0.05) but not with morning cortisol concentrations (r=0.018, df=12, n.s.). The Combat Exposure Scale and Atrocity Scale scores were not intercorrelated (r=0.126, df=12, n.s.) and thus appeared to measure separate dimensions of exposure to stress.

DISCUSSION

The present study demonstrates that patients with PTSD have a substantially greater number of lymphocyte glucocorticoid receptors than normal comparison subjects. These findings are consistent with our previous observations of low 24-hour urinary cortisol excretion in PTSD (1, 2) and provide further evidence for a dysregulation of the HPA axis in PTSD. Furthermore, the receptor changes we observed are opposite of those reported in major depressive disorder (14, 15). In major depressive disorder, changes in HPA function are thought to involve CRF hypersecretion (8, 9), which could occur in response to a decrease in the number of glucocorticoid receptors or sensitivity (10). In contrast, the present data, along with other findings of HPA abnormalities in PTSD, support the possibility of greater negative feedback sensitivity at one or more levels of the HPA axis.

The strong relationship between the number of glucocorticoid receptors and PTSD symptoms as assessed by the Mississippi scale suggests that glucocorticoid receptors may be functionally relevant to PTSD. The significant correlation between the number of glucocorticoid receptors and anxiety symptoms is consistent with the classification of PTSD as an anxiety disorder according to *DSM-III-R*. In contrast, the modest (nonsignificant) correlation between the number of glucocorticoid receptors and Hamilton depression scale scores suggests that changes in the number of glucocorticoid receptors are not likely due to adjunctive symptoms of depression. Related to this, the number of glucocorticoid receptors was not different in PTSD patients with and without comorbid depression.

There were no differences in the number of glucocorticoid receptors or in cortisol concentrations between medicated and drug-free PTSD patients in our study group. This result agrees with the finding of a previous study that there were no differences in the number of glucocorticoid receptors between medicated and nonmedicated depressed subjects (15). It is possible that our inability to detect specific medication effects was due to the heterogeneous nature of the medication status in the patient group. Further study is required to determine the extent to which medications may affect the number of lymphocyte glucocorticoid receptors.

Lymphocyte glucocorticoid receptors and plasma cortisol levels were measured simultaneously to determine diurnal rhythmicity. When the relationship between plasma cortisol levels and the number of glucocorticoid receptors was examined, no significant correlations were observed in the patient group, the comparison group, or both groups combined. The lack of any relationship between the number of glucocorticoid receptors and plasma cortisol levels could be due to the use of a single cortisol measurement, which may not be an accurate reflection of overall HPA activity due to the episodic nature of cortisol secretion. Other studies measuring the number of glucocorticoid receptors and plasma cortisol levels have also failed to find significant relationships between these measures when using a single cortisol measurement (14, 15, 23, 24). Analysis of the diurnal variation, however, revealed that changes in glucocorticoid receptor levels paralleled diurnal changes in cortisol levels (i.e., the number of glucocorticoid receptors was greater in the morning than in the afternoon). The lack of an inverse relationship between the number of receptors and agonists indicates that the steady-state number of cytosolic glucocorticoid receptors could be influenced by fluctuations in plasma cortisol levels occurring hours before the actual sampling time. The equivalent cortisol levels between the two groups at the time of blood sampling suggest, however, that the greater number of glucocorticoid receptors in the patients with PTSD cannot simply be attributed to cortisol occupation and/or translocation of the cytosolic receptor.

Homologous regulation of glucocorticoid receptors by glucocorticoids has been demonstrated in a variety of tissues (12, 25). However, it is evident that the regulation of glucocorticoid receptors by glucocorticoids is region-specific and not necessarily uniform in all tissues (11, 26). The regulation of lymphocyte glucocorticoid receptors by glucocorticoids in humans has been examined in several studies. Exogenous administration of glucocorticoids can lower the number of lymphocyte glucocorticoid receptors in normal subjects and in patients with leukemia (27). However, regulation of lymphocyte glucocorticoid receptors by endogenous glucocorticoids has not been firmly established. Thus, patients with endocrine disorders resulting in markedly high levels of cortisol (i.e., Cushing's disease) or very low circulating levels of cortisol (i.e., Addison's disease) have relatively normal levels of lymphocyte glucocorticoid receptors (28, 29). In contrast, in psychiatric disorders such as major depressive disorder and anorexia nervosa, which are generally characterized by greater cortisol secretion within the endocrinologically "normal" range, studies have tended to find lower numbers of lymphocyte glucocorticoid receptors. However, as already noted, no significant correlation between the number of glucocorticoid receptors and plasma cortisol levels were observed in those studies (14, 15, 24). Clearly, further studies are required to establish the extent to which lymphocyte glucocorticoid receptors are regulated by endogenous cortisol levels under normal and pathological conditions. In particular, use of 24-hour urine samples may be the measure of choice in elucidating such a relationship. On the other hand, heterologous regulation of lymphocyte glucocorticoid receptors by a variety of nonglucocorticoid factors (30, 31) makes a simple relationship between cortisol levels and the number of glucocorticoid receptors unlikely.

The relationship between the large number of lymphocyte glucocorticoid receptors and neuronal glucocorticoid receptors in PTSD is not known. However, some similarities between lymphoid and neuronal glucocorticoid receptors have been reported in animal studies. For example, high concentrations of glucocorticoid receptors are found in both types of tissues, which are similar in receptor affinity and steroid specificity (32). Lymphoid and neuronal glucocorticoid receptors also share some common regulatory mechanisms; for example, adrenalectomy in rats produces greater numbers of both lymphocyte and hippocampal glucocorticoid receptors (22, 31). If the large number of lymphocyte glucocorticoid receptors in PTSD similarly reflects a large number of hippocampal glucocorticoid receptors, then the HPA abnormalities observed in PTSD could, in fact, be related to greater feedback sensitivity to glucocorticoids. Hippocampal glucocorticoid receptors in particular play a prominent role in stress-induced feedback inhibition of the HPA axis (32) and, therefore, may be an important aspect of HPA dysregulation in PTSD.

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Salivary Cortisol Levels and Their Correlation With Plasma ACTH Levels in Depressed Patients Before and After the DST

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Objective: The aim of this work was to study the clinical utility of salivary cortisol concentrations in a group of depressed patients undergoing the dexamethasone suppression test (DST) and the correlation of these concentrations with plasma ACTH levels. Method: Twenty outpatients from the psychiatric department of a Barcelona hospital who were diagnosed as having nonendogenous (N=9) or endogenous (N=11) depression according to DSM-III criteria and the Newcastle scale participated in the study. The comparison group consisted of 12 healthy volunteers. Blood and saliva samples were taken before and after administration of 1 mg of dexamethasone Salivary cortisol and plasma ACTH concentrations were determined by direct iodine-125 radioimmunoassay with commercial kit reagents. Results: Predexamethasone salivary cortisol concentrations were significantly higher in the group with endogenous depression than in the comparison group. A significant correlation was obtained between plasma ACTH and predexamethasone salivary cortisol levels in the group with nonendogenous depression and in the comparison subjects. Conclusions: These preliminary findings indicate that salivary cortisol could substitute for plasma cortisol in clinical studies in which the DST and hypercortisolemia are evaluated. The lack of correlation between ACTH and cortisol levels in saliva in the group of endogenously depressed patients could indicate a disturbance in the regulation of cortisol secretion in major depression.

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The measurement of hormones in saliva has rapidly developed in the past few years, but there has been general agreement on the clinical value of salivary assays of only a few hormones. Data obtained on other hormones are still inconclusive for clinical purposes. Cortisol has received the attention of a considerable number of studies, and the demonstration of the clear relation between saliva levels and plasma (total and free) levels, the lack of salivary flow rate effect, and other factors have led several groups of investigators to conclude that determinations of salivary hormone levels can replace plasma measurements in studies of adrenal cortical function (1).

A large number of studies have strongly suggested abnormal activity of the hypothalamic-pituitary-adrenal (HPA) axis in depressive illness (2), and plasma cortisol levels have been extensively used in psychiatry to evaluate this neuroendocrine disturbance. Since the description by Poland and Rubin (3) of salivary cortisol levels in endogenously depressed patients undergoing the dexamethasone suppression test (DST), a few reports have been published on this subject (4–6), and the data show that when salivary levels are used, the sensitivity and specificity of the test are similar to or higher than those obtained when plasma levels are measured. Also, in these studies salivary concentrations of cortisol were compared with endogenous features of depression (6) and with cortisol levels of patients with other psychiatric disorders (4).

On the other hand, measurements of plasma ACTH and their correlation with plasma cortisol levels have been described in depressed patients, and the results demonstrate nonsignificant differences from the results in normal subjects (7, 8). Since salivary cortisol, like plasma free cortisol, has a more sensitive response to

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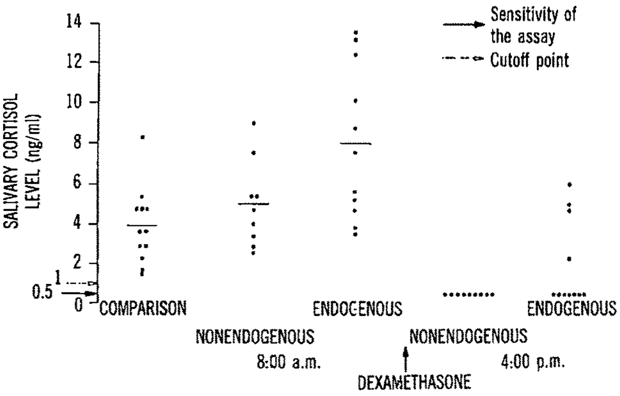
FIGURE 1. Salivary Cortisol Concentrations in 20 Patients With Endogenous or Nonendogenous Depression and 12 Comparison Subjects at Baseline and in the Depressed Patients After 1 mg of Dexamethasone[a]



[a]Bars indicate mean values.

changes in ACTH secretion (9, 10) than total plasma cortisol, we were prompted to investigate the relation between the levels of these hormones in patients with affective disorders.

In this preliminary investigation we studied the clinical utility of salivary cortisol concentrations in a group of depressed patients undergoing the DST and their correlation with plasma ACTH levels.

METHOD

The depressed group consisted of 20 outpatients (15 women and five men), ranging in age from 20 to 65 years, who were referred to the psychiatric department of a hospital in Barcelona. The patients were unmedicated and gave informed consent before participating in the study. According to *DSM-III* criteria, 11 patients were diagnosed as having major depression, and nine were suffering from dysthymic disorder. The 11 patients with major depression were further diagnosed as having the endogenous type according to the Newcastle depression scale (11) criteria (cutoff score of 6), and the nine with dysthymic disorder met the criteria for nonendogenous disorder, since they had scores of 5 or less on the Newcastle scale.

The comparison group consisted of 12 healthy volunteers of both sexes from the hospital staff, aged 25–50 years, who were free from psychiatric or medical illnesses.

On the first day, blood was obtained by venipuncture between 8:00 a.m. and 9:00 a.m. and transferred to precooled siliconized glass tubes containing EDTA disodium as an anticoagulant and aprotinin (500 kallikrein inhibitor units per milliliter) as an antiproteolytic agent. The tubes were centrifuged at 4 °C and the plasma stored at −20 °C until assayed for ACTH concentrations. After blood collection the subject spat directly into a glass tube, the freshly collected saliva (1–2 ml) was centrifuged for 10 minutes at 1500 rpm, and the supernatant was stored at −20 °C until cortisol levels were determined. The patients were given 1 mg of dexamethasone orally at 11:00 p.m., and the next day they returned at 4:00 p.m. for blood drawing and saliva collection to determine plasma ACTH and salivary cortisol levels. On the second day, plasma cortisol concentrations were also measured in samples obtained at 4:00 p.m.

Plasma cortisol levels were determined by direct iodine-125 radioimmunoassay with the Farmos Diagnostica (Turku, Finland) kit reagent, as described previously (12). Salivary cortisol concentrations were measured from nonextracted saliva (100 μl) (4) with the same reagent kit but with the appropriate dilutions of the antibody and standards described in the manufacturer's modified assay method for salivary determinations. The lowest concentration that could be distinguished with 95% confidence was 0.5 ng/ml. The intra-assay coefficient of variation for the method was 3.8% (mean±SD=5.2±0.02 ng/ml; N=12).

Plasma ACTH was measured from nonextracted samples by an iodine-125 radioimmunoassay reagent kit developed by Nichols Institute (San Juan Capistrano, Calif.). Cross-reactivities of the antibody were 0.20% for β-lipotropin, <0.03% for β-melanocyte-stimulating hormone, and <0.10% for β-endorphin. The minimum detectable concentration was 10 pg/ml. Coefficients of intra-assay and interassay variations were 7.8% (mean±SD=55.0±2.5 pg/ml; N=14) and 12.6% (45.0±6.5 pg/ml; N=16), respectively.

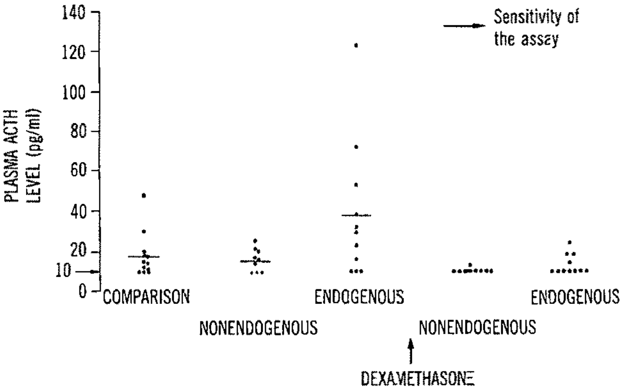
Comparisons between the two subgroups of depressed patients and the comparison subjects were done with the Mann-Whitney U test. Correlations were calculated with Spearman's rank correlation test.

RESULTS

Predexamethasone and postdexamethasone salivary cortisol levels for the two depressed subgroups and baseline salivary cortisol values for the comparison group are shown in figure 1. Before receiving dexamethasone, the endogenously depressed patients had significantly higher cortisol concentrations (mean±SD=8.02±3.81 ng/ml) than the comparison subjects (3.86±1.88 ng/ml) ($U=2.74$, $p<0.01$) and a tendency toward significantly higher concentrations than the nonendogenously depressed patients (4.98±2.13 ng/ml) ($U=1.83$, $p=0.07$). After receiving dexamethasone, four (36%) of the 11 endogenously depressed patients were nonsuppessors (criterion value=1 ng/ml). The same results were obtained when the patients were categorized as nonsuppressors according to their plasma cortisol levels (at least 5 μg/dl) (13). In the group with nonendogenous depression, all patients had cortisol levels lower than the respective salivary and plasma cutoff points (1 ng/ml and 5 μg/dl).

Pre-DST and post-DST ACTH levels for the two depressed subgroups and baseline ACTH values for the comparison subjects are shown in figure 2. Before dexamethasone the mean±SD baseline plasma ACTH concentration of the group with nonendogenous depression (15.88±5.40 pg/ml) and of the comparison group (17.5±9.87 pg/ml) did not differ significantly from that of the group with endogenous depression (37.81±34.32 pg/ml) (U=1.62, p=0.10, and U=1.43, p=0.15, respectively). We obtained a significant correlation between plasma ACTH and predexamethasone salivary cortisol concentrations in the patients with nonendogenous depression (r=0.83, df=8, p< 0.02) and in the comparison subjects (r=0.66, df=11, p<0.03), but the correlation was nonsignificant in the group with endogenous depression (r=−0.02, df=8, p>0.05). After dexamethasone, ACTH values fell below the sensitivity of the assay in 75% (N=15) of the 20 patients. The results were not evaluated statistically.

FIGURE 2. Plasma ACTH Concentrations in 20 Patients With Endogenous or Nonendogenous Depression and 12 Comparison Subjects at Baseline and in the Depressed Patients After 1 mg of Dexamethasone[a]



[a] Bars indicate mean values.

DISCUSSION

When salivary cortisol levels were measured, the percentages of nonsuppressors in the two depressed subgroups we studied were the same as those obtained when plasma cortisol determinations were used. Patients categorized as nonsuppressors according to the standard cutoff level for plasma cortisol (5 μg/dl) were also nonsuppressors when salivary cortisol levels were evaluated (cutoff level of 1 ng/ml). Although more extensive experience is necessary before cutoff salivary cortisol values for the DST that have the same specificity and sensitivity as plasma levels can be defined, our preliminary results are in the range of those described by other authors who have found the best cutoff point to be 0.7 ng/ml (4).

It has been noted that a single nocturnal (11:00 p.m.) measurement of salivary cortisol in patients not undergoing the DST could demonstrate the higher cortisolemia which exists in primary depressive disorders (14). Our data show that morning (8:00 a.m.) predexamethasone salivary concentrations are significantly higher in endogenously depressed patients than in normal comparison subjects. Statistical analysis of the baseline salivary cortisol values for the two depressed subgroups showed a clear tendency toward a significant difference, and the data are in accord with the results found in our laboratory for plasma cortisol when a larger number of patients were evaluated (12).

Although the difference was not statistically significant, we found a definite trend toward greater baseline plasma ACTH values in the patients with endogenous depression than in those with nonendogenous depression and the comparison subjects, in agreement with earlier reports of greater ACTH secretion in major depressive illness (2). To our knowledge, a correlation between salivary cortisol and plasma ACTH levels has not previously been described in depressed patients. In this preliminary study we obtained significant correlations between the two hormone levels at baseline for the patients with nonendogenous depression and the comparison subjects. The correlation between plasma ACTH level and total cortisol level is difficult to demonstrate even in normal subjects (7, 8), and our results could be explained by the advantages of salivary cortisol measurements over plasma cortisol determinations in response to ACTH changes (9, 10). We were not able to find a significant correlation between baseline levels of salivary cortisol and plasma ACTH in the endogenously depressed patients, results which may in part be interpreted in the context of recent reports on cortisol secretion. A number of studies in several animal species have shown that other substances, rather than ACTH, may stimulate or modulate adrenal corticosteroidogenesis (15–17). The exclusive role of ACTH in the regulation of cortisol secretion in human beings has been questioned (18), and the biochemical alterations in depressed patients at the brain or pituitary level could influence cortisol secretion through a peripheral site of action or through the autonomic innervation of the adrenal cortex.

We conclude that, since saliva is a biological fluid which offers a number of advantages in clinical testing, measurement of salivary cortisol levels before and after dexamethasone could be a reliable and practical technique in psychiatry for performing the DST and for gathering evidence on hyperactivity of the HPA axis in major depression.

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Treatment of Seasonal Affective Disorder With Green Light and Red Light

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Objective: This study sought to determine whether an equal photon density of green light is superior to red light in treating seasonal affective disorder. Method: After recruitment through the media, 20 outpatients with seasonal affective disorder participated in a balanced-order crossover trial of 1 week of green light therapy compared with 1 week of red light therapy. Each treatment consisted of 2 hours of daily light treatment at home in the early morning. Ultraviolet light was excluded from both treatment conditions. The photon densities of the two treatments (2.3×10^{15} photons/sec per cm^2) were similar to those used in previous studies of therapy with 2500-lux white light. Fourteen patients completed the study. At least 1 week separated each treatment period to allow time for relapse. Effectiveness of treatment was assessed by analysis of variance of changes in ratings on the Hamilton Rating Scale for Depression. Results: Although patients' expectations of the two treatments were similar, green light induced greater antidepressant effects than red light. A Sequence by Color interaction was also demonstrated. Conclusions: Green light provides a treatment effect superior to that of red light and similar to that seen in previous studies with white light. These results are consistent with the hypothesis that retinal photoreceptors mediate the antidepressant response in seasonal affective disorder. Identifying optimal wavelengths for light treatment is important in optimizing phototherapy efficacy.

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Seasonal affective disorder (1) may be treated with white light (2). A recent study (3) suggested that white light is more therapeutic for this disorder than red or blue light. No trial, however, has established whether a specific wavelength band can treat the disorder effectively.

We conducted a crossover study of the antidepressant effects of green versus red light in seasonal affective disorder. We chose green because retinal photoreceptors are more sensitive to green wavelengths than to any other band of visible light (4), and we chose red because of its previous use as a plausible placebo for depressed patients (3, 5).

METHOD

The subjects were recruited through the media. Criteria for entry into the study were 1) a diagnosis of seasonal affective disorder (1), 2) a score of at least 13 on the 21-item Hamilton Rating Scale for Depression, 3) no phototherapy for 10 days before the study, and 4) no previous experience of therapy with green or red light. All subjects gave informed consent. They kept their sleep schedules and medication regimens, if any, constant for 2 weeks before the study and throughout the trials.

In winter, during different 7-day periods, these depressed patients were exposed in their homes to different daily 2-hour treatments with colored light between 5:30 a.m. and 9:00 a.m. The treatments were administered in a balanced, randomized crossover design with at least 7 days between treatment periods. Raters who were blind to the order of the treatments evaluated patients weekly with a structured interview

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TABLE 1. Scores on the 21-Item Hamilton Rating Scale for Depression of 14 Patients With Seasonal Affective Disorder Treated With Green and Red Light

	Hamilton Depression Score			
	Green Light		Red Light	
Condition/ Patient	Baseline	After 1 Week	Baseline	After 1 Week
Green light first				
1	28	16	14	4
2	17	1	12	12
3	24	13	14	21
4	18	6	18	19
5	13	2	12	3
6	18	12	12	18
7	27	15	15	6
Group				
Mean	21	9	14	12
SD	6	6	2	8
Red light first				
8	13	12	21	15
9	18	5	18	4
10	12	21	13	21
11	29	4	26	16
12	13	0	18	4
13	19	7	23	3
14	12	12	17	18
Group				
Mean	17	9	19	12
SD	6	7	4	8
Total				
Mean	19	9	17	12
SD	6	6	4	7

that included the 21-item Hamilton depression scale and an atypical symptom subscale (6). Patients' Hamilton scale scores were required to be 12 or higher before the second treatment—lower than required for the initial treatment, since depression frequently takes more than 1 week to relapse to pretreatment levels. If a patient's Hamilton score was less than 12 after 1 week, additional weeks were allowed for relapse.

In the two lighting conditions we used equal quanta (2.3×10^{15} photons/sec per cm^2) of red or green light—similar to those used in previous studies of therapy with 2500-lux white light (1–3, 7). All lamps (fluorescent 40-W red and fluorescent 40-W green) were "burned in" and housed in portable fixtures with clear pyramidal diffusers and ultraviolet and gelatin filters. The red and green light units emitted half-peak bandwidths of 615–685 nm and 505–555 nm, respectively. To balance photon density, patients sat 30 inches from a unit containing eight green bulbs in one condition and 20 inches from a unit containing 16 red bulbs in the other.

Patients were not informed about the color of light they would receive each week until each treatment condition began. After experiencing the treatment condition briefly, each patient completed an expectation assessment form (8). We assessed color vision weekly with a Nagel anomaloscope, the Farnsworth-Munsell 100-hue test, or both.

We examined changes in mood by means of analysis of variance (ANOVA) with one grouping factor (sequence) and one repeated measure (color), and we compared changes in scores on the structured interview by means of t tests. We evaluated expectations with the Wilcoxon signed-ranks test and Spearman rank-order correlations.

RESULTS

Ten women and four men completed the experiment. Ten of these patients met criteria for unipolar depression, and four met criteria for bipolar II depression. No patient showed evidence of abnormal color vision. Seven patients were assigned to each color treatment first. Six other patients did not complete the study because of noncompliance, medical illness, or failure to relapse after the first treatment condition.

The ANOVA of Hamilton depression scores showed a color effect ($F=6.2$, $df=1, 12$, $p<0.05$) and a Sequence by Color interaction ($F=6.2$, $df=1, 12$, $p<0.05$) (table 1). The interaction occurred because patients treated with red light first had equal improvements in depression scores in both conditions (8±11 with green and 8±10 with red), whereas patients treated with green light first had a much larger improvement with green light (11±3) than with red light (2±7). Hamilton depression ratings before the two treatments were not significantly different. Using t tests, we found that changes in Hamilton score were significant for the green light condition only (green light, $t=4.5$, $df=13$, Bonferroni $p<0.005$; red light, $t=2.1$, $df=13$, Bonferroni $p>0.10$, $p=0.58$). The mean ±SD change in atypical symptom score with green light was 6±7 points ($t=3.5$, $df=13$, Bonferroni $p<0.05$), and the change with red light was 7±7 points ($t=3.5$, $df=13$, Bonferroni $p<0.05$). The ANOVA for atypical symptoms showed no sequence, color, or interaction differences.

Expectations of response in both conditions were similar and largely positive. There was no correlation between expectations of improvement and changes in Hamilton depression score in either condition.

DISCUSSION

The antidepressant effect of green light was superior to that of red light. The magnitudes of change in Hamilton depression score with green and red light resemble those observed in previous studies in which an active form of phototherapy was compared with an inactive one (2).

Since ultraviolet radiation was screened out from both the red and the green light sources, this study suggests that ultraviolet radiation is not critical to phototherapy in seasonal affective disorder. Since ultraviolet radiation has been associated with adverse effects, it is important for clinicians to know that ultraviolet is probably unnecessary for the antidepressant effects of phototherapy. We cannot rule out the possibility, however, that phototherapy for seasonal affective disorder might be more effective with a certain amount of ultraviolet radiation. Similarly, the failure of red light as an antidepressant in this study should not be viewed as proving that it is ineffective, but only that it was ineffective in this paradigm.

The effectiveness of green light is consistent with the hypothesis that retinal photoreceptors mediate the antidepressant response in seasonal affective disorder. In view of these experimental results, it seems logical to focus the search for biological mechanisms of phototherapy on processes involving photoreceptors.

We also explored the relation between expectations of and responses to phototherapy. Expectations of the two types of phototherapy poorly predicted patients' responses to treatment. This suggests that expectations did not account for most of the therapeutic effect of green light that we saw in this study.

A Sequence by Condition interaction has been found in several studies of seasonal affective disorder. One interpretation of the interaction we found in our study is that the placebo effect of red light was almost as powerful as green light in the first treatment condition.

Several properties of phototherapy that are critical for its therapeutic effect have been identified. Intensity (1) and duration (2) appear to be important. Early morning may be the most effective time for treatment (2, 7), although this hypothesis is controversial. In this study we addressed wavelength. It now seems that ultraviolet-free green light will provide a treatment effect similar to that seen with white light in earlier studies.

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Cardiovascular Effects of Bupropion in Depressed Patients With Heart Disease

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Objective: The cardiovascular effects of therapeutic plasma levels of tricyclic antidepressants in depressed patients with and without preexisting cardiac disease have been well characterized and include orthostatic hypotension and conduction delay. Bupropion, structurally unrelated to tricyclic antidepressants, is relatively free of cardiac side effects in depressed patients without cardiac disease. However, it is unknown whether bupropion is safe for depressed patients with preexisting heart disease, so the authors studied the cardiovascular effects of bupropion in such patients. Method: The subjects were 36 inpatients with DSM-III *major depression and preexisting left ventricular impairment (N=15), ventricular arrhythmias (N=15), and/or conduction disease (N=21). The patients continued their cardiac drug regimens and received bupropion for 3 weeks (mean±SD dose=442±47 mg/day). Cardiovascular functioning was measured by pulse, blood pressure, high-speed ECG, 24-hour portable ECG, and radionuclide angiography. Results: Although bupropion caused a rise in supine blood pressure, it did not cause significant conduction complications, did not exacerbate ventricular arrhythmias, had a low rate of orthostatic hypotension, and had no effect on pulse rate. However, bupropion treatment was discontinued for 14% of the patients because of adverse effects, including exacerbation of baseline hypertension in two patients. Conclusions: The cardiovascular profile of bupropion may make this drug a useful agent in the treatment of the depressed patient with preexisting cardiovascular disease. Further studies, with longer durations of bupropion treatment and more subjects, are needed to confirm these findings.*

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There has been longstanding concern over the cardiovascular effects of tricyclic antidepressants, originally prompted by the observation that patients who took overdoses of tricyclic antidepressants died from heart block and/or arrhythmias (1). Over the past 15 years, a number of careful studies have established the characteristic effects and cardiovascular complications of tricyclic treatment in depressed patients with and without heart disease (2–4).

Bupropion is a new antidepressant of the aminoketone class that is structurally unrelated to the tricyclic antidepressants, and it is relatively free of cardiac side effects in healthy depressed patients (5, 6). However, it was unknown whether bupropion is safe for depressed patients with preexisting heart disease. Therefore, the goal of this study was to evaluate the cardiovascular effects of bupropion in depressed patients with preexisting congestive heart failure, conduction disease, and/or ventricular arrhythmias. Some of these data have been previously reported (7).

METHOD

Subjects

This paper contains the findings of a 3-year study of bupropion in depressed patients with cardiovascular disease. All of the data reported in this study were obtained from inpatients admitted to the Affective Disorders Research Unit of the New York State Psychiatric Institute who had both cardiac disease and *DSM-III* major depression severe enough to warrant

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treatment with an antidepressant medication. On admission, each patient was examined by a psychiatrist and a cardiologist. To be included in this study, a patient had to have 1) a history of congestive heart failure and/or an enlarged heart according to chest roentgenogram (cardiac thoracic ratio greater than 0.5 in the frontal view), 2) evidence of bundle branch block, defined as a QRS interval greater than 0.10 seconds, or 3) more than 10 ventricular premature depolarizations per hour, as determined by two separate, continuous 24-hour ECG recordings. All patients gave informed consent, and the study was approved by the Institutional Review Board of the New York State Psychiatric Institute/Columbia University Department of Psychiatry.

Thirty-six patients met the protocol criteria: 15 with congestive heart failure, 21 with conduction disease, and 15 with ventricular arrhythmias; some patients had more than one cardiac problem concurrently. There were 14 men and 22 women, and their mean±SD age was 69±9 years (range, 49–86 years).

Procedure

Treatment with all psychotropic drugs except benzodiazepines was discontinued; stable doses of digoxin, diuretics, and antihypertensives were maintained. Each patient's cardiac drug regimen was maintained for 7 to 10 days, and then baseline cardiovascular measurements were obtained. Left ventricular ejection fraction was derived from first pass radionuclide angiography, as previously described by Goldman et al. (8). High-speed ECG (2) was used to measure duration of PR and QRS intervals (in milliseconds), and 24-hour ECG recordings with a movable monitor were used to determine 1) intermittent periods of higher-degree AV block in patients with bundle branch block that were not evident on the ECG, 2) ventricular arrhythmias, and 3) mean 24-hour pulse rate.

Blood pressure was measured three times daily. Supine blood pressure was measured after at least 5 minutes of quiet rest. After the patient stood for 1 minute, the blood pressure measurement was repeated. To obtain mean supine and standing blood pressure measurements for the predrug and drug periods, the daily blood pressure readings were pooled and averaged for the drug-free week and for the third week of drug treatment. Orthostatic drop is defined as the supine systolic blood pressure minus the standing systolic blood pressure. For the purposes of this study, a patient was considered to have orthostatic hypotension that required discontinuation of drug treatment if 1) an orthostatic drop of 50 mm Hg or more was recorded on 3 separate days and/or 2) the patient was unable to maintain a standing position because of symptoms associated with an orthostatic drop of 30 mm Hg or more.

After baseline cardiac measurements were obtained, bupropion treatment was started. The initial dose was 150 mg/day, given by mouth, which was increased to 450 mg/day by day 7. Drug was administered in three equal doses during the day. In two cases the dose was raised above 450 mg/day (550 mg for one patient, 600 for the other) because only partial response was noted (these doses are higher than currently recommended). The mean±SD daily dose of bupropion was 442±47 mg (range, 350–600 mg). The plasma level of drug, based on a sample obtained 12 hours after the last dose, was measured 2 weeks after the patient reached the full dose. This produced an average concentration of bupropion and its major metabolites of 3719±1530 ng/ml at steady state, as determined with the method of Cooper et al. (9). After 3 weeks of drug treatment, the cardiovascular measures were repeated.

The results are expressed as mean±SD. For statistical analysis, we calculated mean change (±SD) and used paired t tests to compare baseline measurements with those during bupropion treatment. Statistical significance was defined as $p<0.05$.

RESULTS

Pulse rate measurements were available at baseline and during bupropion treatment for 34 of the 36 patients in the study. The mean 24-hour pulse rate at baseline was 74.8±11.9 bpm, compared with 76.6±10.4 bpm with bupropion (mean change, 1.8±10.2 bpm; $t=-1.03$, $df=33$, n.s.).

As shown in table 1, bupropion induced a statistically significant increase in lying systolic and diastolic blood pressures. The mean standing systolic and diastolic blood pressures were not significantly different during bupropion treatment. Bupropion induced a statistically significant, but clinically insignificant, increase in orthostatic drop (table 1). However, one patient developed dizziness and fell in conjunction with an orthostatic drop of 40 mm Hg, and bupropion was discontinued.

Effects on Cardiac Functioning

In the 15 patients with impaired left ventricular function, the mean ejection fraction during the baseline period was 34%±13% (range, 11%–54%). At maximum dose of bupropion the mean ejection fraction was 32%±14% (range, 16%–64%), and the mean change between the baseline and bupropion periods was 2%±6% ($t=1.18$, $df=14$, n.s.). Thus, bupropion had no significant effect on ejection fraction.

We analyzed separately the data on orthostatic drop in the 15 patients with impaired left ventricular function. Their orthostatic drop was 3±7 mm Hg before treatment and 3±10 mm Hg with bupropion ($t=0.16$, $df=14$, n.s.). No patient in this group stopped taking bupropion because of orthostatic hypotension.

For the 21 patients who had preexisting conduction disease, the mean PR interval was 0.162±0.02 second

TABLE 1. Blood Pressure Before and During Bupropion Treatment in 36 Patients With Major Depression and Cardiac Disease

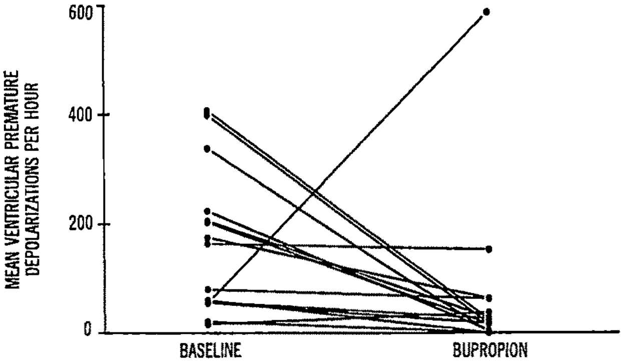
	Blood Pressure (mm Hg)						Paired t Test	
	Baseline		Bupropion		Change		t	
Measure	Mean	SD	Mean	SD	Mean	SD	(df=35)	p
Supine blood pressure								
Systolic	140	16	145	20	5	10	−2.79	<0.01[a]
Diastolic	76	7	79	9	3	5	−3.00	<0.005[a]
Standing blood pressure (after 1 minute)								
Systolic	136	18	137	19	1	10	0.70	n.s.
Diastolic	80	8	82	9	2	6	1.93	n.s.
Orthostatic drop	4	9	7	12	4	9	2.57	<0.02[a]

[a] The magnitude of drug effect, although statistically significant, was not clinically significant. However, the relatively small changes in the group means did not imply safety for all patients. One patient developed symptomatic orthostatic hypotension, and two patients developed significant systolic hypertension (see text).

at baseline and 0.167±0.03 during drug treatment (mean change, 0.005±0.01 second; t=−2.02, df=20, p=0.06). The mean QRS interval was 0.126±0.01 second before treatment and 0.128±0.02 with drug (mean change, 0.002±0.01; t=−0.94, df=20, n.s.). There were no significant conduction complications and no evidence of a higher degree of AV block during drug treatment than at baseline.

Fifteen patients had 10 or more ventricular premature depolarizations per hour during two continuous 24-hour ECG recordings: 164±133 per hour at baseline and 69±149 at the maximum dose of bupropion (mean change, −95±222; t=1.66, df=14, p=0.12). One patient had a mean of 56 ventricular premature depolarizations per hour at baseline, which increased to 588 per hour with bupropion and subsequently to 1439 per hour after drug treatment. This fluctuation probably represents day-to-day variability in the frequency of ventricular premature depolarizations. When this patient was excluded from the data set, the remaining 14 patients had 172±134 ventricular premature depolarizations per hour at baseline and 32±40 with drug, i.e., 82% suppression (mean change, −140±144; t=3.64, df=13, p<0.005) (see figure 1).

FIGURE 1. Ventricular Premature Depolarizations Before and During Bupropion Treatment in 15 Depressed Patients With Heart Disease



Complications

Five patients could not complete treatment because of adverse effects. One patient had psoriasis and developed a skin rash after 10 days at a dose of 450 mg/day of bupropion. The rash resolved after cessation of bupropion treatment. The results of a skin biopsy were consistent with a drug eruption. For two other patients, both of whom had mild hypertension at baseline, bupropion treatment was discontinued because of further elevation of systolic and diastolic blood pressures. One had a mean baseline standing blood pressure of 165/92±12/12 mm Hg and a highest single recording at baseline of 188/108 mm Hg. During bupropion treatment the systolic blood pressure increased to 180–200 mm Hg frequently and reached a maximum of 214/120 mm Hg. Bupropion treatment was discontinued, and the average blood pressure returned to the baseline range (170/86±14/10 mm Hg), and the maximum was 178/90 mm Hg. Another patient's mean baseline standing blood pressure was 163/89±18/9 mm Hg, and the highest single baseline recording was 204/96 mm Hg. After 2 weeks of taking bupropion, the patient's systolic blood pressure was frequently in the 190–210 mm Hg range, and the maximum was 210/110 mm Hg. Again, bupropion treatment was discontinued, and after 3 days the average standing blood pressure was 151/88±8/6 mm Hg, and the maximum was 160/98 mm Hg. A fourth patient, who had a history of hypertension but did not have impaired left ventricular function, became dizzy and fell in association with a 40 mm Hg orthostatic drop after 8 days of treatment. Major orthostatic drops ceased within a day after discontinuation of bupropion treatment. The fifth patient, who had a history of myocardial infarction, syncope, lightheadedness, and New York Heart Association class III stable angina, developed a changing anginal pattern after 19 days of taking bupropion.

While cause-and-effect relationships are difficult to establish, in four of the five cases the adverse conditions resolved after discontinuation of bupropion administration.

DISCUSSION

Previous studies have focused on whether tricyclics are safe for depressed patients with preexisting heart disease, specifically congestive heart failure, conduction delay, or ventricular arrhythmias (10, 11).

A number of investigators have concluded that imipramine, nortriptyline, and doxepin do not have a deleterious effect on left ventricular function (12–14), even in patients with severe preexisting left ventricular impairment. However, the rate of orthostatic hypotension induced by imipramine in the patients studied approached 50% (14), making its use problematic. In contrast, the rate of orthostatic hypotension associated with nortriptyline is much lower (12). Thus, in depressed patients with left ventricular impairment, nortriptyline can usually be used safely even when imipramine treatment has been discontinued because of orthostatic hypotension (12).

With respect to the effect on cardiac conduction, early studies (2) demonstrated that in patients without heart disease, tricyclics, at plasma concentrations effective for treatment of depression, frequently prolong the PR, QRS, and QTc intervals but rarely, if ever, cause symptomatic conduction disturbance. Subsequently, Roose et al. (15) compared the risks of cardiovascular complication at therapeutic plasma tricyclic concentrations in 155 patients with normal ECGs and 41 patients with prolonged PR interval and/or bundle branch block. The prevalence of 2:1 AV block was significantly greater in the patients with preexisting bundle branch block (9%) than in the patients with normal ECGs (0.7%). In an additional 10% of the patients with preexisting bundle branch block, treatment with tricyclics was discontinued because of prolongation of the QRS interval by more than 25%. Thus, although nortriptyline can be relatively safely used to treat depressed patients with left ventricular impairment, all of the tricyclics, including nortriptyline, should be used with caution with patients who have bundle branch disease.

The data reported herein allow comparison of the cardiovascular effects of bupropion in a comparable group of patients. This study had six major findings: 1) bupropion did not affect pulse rate, 2) bupropion caused an elevation in supine blood pressure, 3) bupropion did not affect left ventricular function, even in patients with severe preexisting left ventricular impairment, 4) bupropion induced orthostatic hypotension in only one of 36 patients with cardiovascular disease, but in none of the patients with impaired left ventricular function, 5) bupropion did not significantly prolong cardiac conduction or induce higher degrees of AV block in patients with preexisting bundle branch block, and 6) bupropion did not exacerbate preexisting ventricular arrhythmias and, indeed, may have had some antiarrhythmic effect.

Thus, when treating a depressed patient with severe heart disease, bupropion may have some advantages over tricyclic antidepressants. These are, most notably, minimal orthostatic hypotension and lack of prolongation of intraventricular conduction. In addition, in the limited number of bupropion overdose cases to date, there have been no major cardiovascular complications (data on file at Burroughs Wellcome).

However, conclusions regarding the relative safety of bupropion treatment for patients with preexisting cardiovascular disease must be tempered by recognition of the limitations of our study. We have reported the cardiovascular effects of bupropion over a 3-week treatment period. It is possible that over a longer period of treatment for depression other effects might emerge. In addition, bupropion may have uncommon but important cardiovascular effects that we did not detect in our small study group. Lastly, 14% of our patients, who had both severe depression and significant cardiac disease, were unable to tolerate the medication. Of particular concern were two patients with preexisting hypertension who had significant increases in blood pressure that resolved after bupropion treatment was discontinued. Overall, we found a modest but statistically significant rise in blood pressure with bupropion. The question remains whether there is a subpopulation who are particularly sensitive to the hypertensive effect of the drug.

The cardiac advantages of bupropion must be weighed against other clinical considerations. Specifically, because of the well-established relationship between plasma concentration and clinical outcome for a number of the standard tricyclic antidepressants (16), tricyclics can be used with greater effectiveness than can newer compounds for which such a relationship has not been established. Furthermore, while we have considered bupropion from a cardiovascular point of view, bupropion has its own profile of adverse effects; of these, seizures have been a particular concern (17).

In the 3 years of this study, five patients who could not tolerate tricyclics because of cardiovascular side effects were treated and maintained with bupropion. Because of such patients, bupropion may be a clinically important addition to the antidepressant armamentarium.

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Controlled Discontinuation of Benzodiazepine Treatment for Patients With Panic Disorder

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Objective: The purpose of this study was to compare the effects of discontinuing treatment with intermediate- and long-acting benzodiazepines. Method: Fifty patients with panic disorder who had taken part in a double-blind treatment study and had responded to alprazolam, diazepam, or placebo for 8 months were asked to stop taking these medications gradually. Results: After a relatively rapid dose reduction, the majority of patients relapsed. Rebound anxiety and withdrawal symptoms were identified in a substantial minority of patients. Those who were taking alprazolam showed earlier and more intense rebound anxiety and withdrawal symptoms than did the patients who received diazepam. Both the level of pretreatment anxiety and the drug the patient was taking predicted the level of anxiety when drug treatment was discontinued. Conclusions: The findings indicate that withdrawal phenomena commonly occur after patients stop taking benzodiazepines and that they are more frequent after discontinuation of treatment with shorter-acting drugs.

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It is clear that we now have effective pharmacologic treatments for panic disorder; not so clear is the long-term efficacy and safety of these treatments. The issue is important because panic disorder is a chronic illness. In fact, despite continuing treatment, 90% of the patients in a recent study (1) remained symptomatic after 3 years. Other follow-up studies of patients with panic disorder and agoraphobia have had similar findings (2–8). Consequently, drug treatments that are effective may be administered for long periods, causing many to wonder what the long-term benefits and risks of such treatments are (9). Of course, the major concern regarding long-term benzodiazepine use is dependence, both psychological and physical (10, 11).

Alprazolam is a high-potency trizalobenzodiazepine that has been shown to be effective in the treatment of panic disorder (12, 13). Its use for this condition has been studied extensively, and several investigators have looked at what happens when treatment with the drug is discontinued (14–16). For instance, Fyer et al. (17) observed a rapid return of panic attacks and the development of withdrawal symptoms in a series of patients who stopped taking alprazolam after about 6 months. Also, Pecknold et al. (18) discontinued alprazolam treatment of 60 panic patients who had taken an average of nearly 5 mg/day for 8 weeks. Tapering of the drug over 4 weeks resulted in rebound of panic attacks in 27% of the subjects and a withdrawal syndrome in 35%. In another placebo-controlled study, Roy-Byrne et al. (19) compared the discontinuation of alprazolam with that of diazepam after these drugs had been taken by panic patients for 6 weeks. After an initial taper, abrupt discontinuation of drug treatment resulted in a higher prevalence of relapse and rebound in the patients taking alprazolam than in those taking diazepam. In all of these studies alprazolam treatment was discontinued relatively rapidly.

We report the results of a double-blind comparison of the gradual discontinuation of alprazolam, diazepam, and placebo administration in 50 patients with panic disorder who had taken these drugs for 8 months.

METHOD

Subjects

This study involved a subgroup of patients with panic disorder who had participated in a controlled treatment study, the results of which will be reported elsewhere. The panic disorder subjects were recruited through the news media and screened with the Structured Clinical Interview for DSM-III (SCID) (20). Each

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was required to meet the *DSM-III-R* criteria for panic disorder and to have had at least one panic attack per week for 3 weeks. Patients were excluded if they had major physical or psychiatric illnesses, including schizophrenia, bipolar disorder, melancholia, dementia, or alcohol abuse within the past 6 months. Patients with major depression were excluded if the onset preceded that of panic disorder or if depressive symptoms dominated the clinical picture.

At baseline, information concerning demographic and additional illness variables was recorded. The demographic information included age, sex, marital status, and social class according to Hollingshead's Two-Factor Index of Social Position (21). We used the SCID to separate the patients into panic disorder subtypes (uncomplicated, limited phobic avoidance, and extensive phobic avoidance) according to a preliminary draft of *DSM-III-R* (Oct. 5, 1985), and patients with major depression (current or past) were identified. Using the Structured Interview for DSM-III Personality Disorders (22), we identified subjects with any *DSM-III* personality disorder. In addition, we recorded the duration of illness for each subject.

After at least a week without any psychotropic medication, the patients were randomly assigned to alprazolam, diazepam, or placebo. Capsules containing 1 mg of alprazolam, 10 mg of diazepam, or placebo were administered in double-blind fashion. The dose was adjusted to achieve maximum benefit within the limits of tolerance. During the initial phase the patients were seen weekly; thereafter, the interval was gradually extended to every other month. During each visit the Hamilton Anxiety Rating Scale (23) and Self-Rated Anxiety Scale (24) were administered. Also recorded were the frequency of panic attacks (three or more symptoms) during the previous week and an estimate of improvement on an 11-point scale of global improvement (0=very bad, could not be worse; 5=no change; and 10=major improvement, back to normal) (12).

Originally, 121 patients were enrolled in the treatment study, which lasted 8 weeks. At the end of that period, the patients who had responded to the study medication were invited to continue taking that medication under double-blind conditions. Sixty-two of the original participants elected to continue taking medication for 6 months and were eligible to take part in the discontinuation study. Of these 62, 12 dropped out of the treatment study before dose reduction was to have begun. All but six of the remaining 50 subjects, who completed at least 1 week of dose reduction, had been taking the study medication for 8 months.

Twenty-four women and 26 men took part in the discontinuation study; all gave informed consent. Their mean±SD age was 39.1±9.8 years. Nineteen subjects met the *DSM-III-R* criteria for extensive phobic avoidance, 22 met the criteria for limited phobic avoidance, and nine were diagnosed as having uncomplicated panic disorder. Nineteen subjects also met the criteria for major depression (current or past). The median duration of illness was 9.5 years. At baseline the mean±SD Hamilton anxiety score was 19.6±8.3, and at the end of the treatment study it was 9.2±8.6. The mean number of panic attacks per week was 5.4±7.9 at baseline and 0.5±1.0 at the end of the treatment study. The medication groups and their mean doses at the end of the treatment study were as follows: alprazolam: N=25, 4.1 mg/day; diazepam: N=19, 34.0 mg/day; placebo: N=6, 5.5 capsules/day. The subjects taking alprazolam did not differ significantly from those taking diazepam with respect to any baseline demographic or illness variable.

Procedure

At the end of the treatment study the patients were asked to reduce the dose of medication by 1 capsule every 3 days until the dose reached 2 capsules/day. At that point, half-strength capsules of alprazolam (0.5 mg) and diazepam (5 mg) were substituted for the original capsules and the dose of drug or placebo was reduced at the same rate (1 capsule every 3 days). The start of the taper was adjusted so that the last dose of study medication would coincide with a regularly scheduled visit. During the discontinuation study patients were seen weekly, and visits were continued until the subjects had been without medication for at least 2 weeks.

The assessments that had been made during the treatment study were continued throughout the dose reduction and discontinuation (12). We also made weekly global ratings of the severity of anxiety symptoms (absent, mild, moderate, severe, or extreme), the relationship of anxiety symptoms to those at baseline (much better, better, the same, worse, or much worse), the occurrence of new symptoms, the occurrence of unplanned telephone contacts, and failure to adhere to protocol. At baseline, at the end of the treatment study, and weekly during the period of dose reduction, a withdrawal symptom checklist was completed. This 53-item checklist, containing both anxiety and benzodiazepine withdrawal symptoms, was developed by M. Liebowitz (personal communication, 1985).

Because the patients were taking doses ranging from 1 to 10 capsules daily, the time required for discontinuing the study medication varied from 1 to 5 weeks. For this analysis, however, we included seven data points, the first two of which were baseline and the end of the treatment study. The other points were the last 3 weeks of dose reduction and the first 2 weeks after discontinuation. Because a large number of subjects dropped out, we analyzed both the available data and data modified by endpoint imputing (except for the second week of no medication) (12). Endpoint imputing involves using the last scores recorded for subjects who dropped out to replace missing values later in the study. In most instances the results obtained with the two methods were similar, and we have included those obtained with endpoint imputing to minimize the loss of data.

TABLE 1. Outcome of Medication Discontinuation for Panic Disorder Patients Who Responded to Alprazolam, Diazepam, or Placebo

Outcome	Aprazolam (N=25)		Diazepam (N=19)		Placebo (N=6)		Alprazolam Versus Diazepam	
	N	%	N	%	N	%	χ^2 (df=1)	p
Relapse (comparison with end of treatment study)								
Increase in anxiety of ≥100%	16	64.0	12	63.2	3	50.0	0.00	0.95
Increase in panic attacks of ≥100%	19	76.0	13	68.4	3	50.0	0.31	0.58
Decrease in global improvement ≥2 points	21	84.0	15	78.9	4	66.7	0.19	0.67
Rebound (comparison with before treatment)								
Increase in anxiety of ≥50%	11	44.0	3	15.8	0	0.0	3.96	0.05
Increase in panic attacks of ≥100%	10	40.0	4	21.1	1	16.7	1.79	0.18
Global improvement score ≤3 (range=0–10)	12	48.0	4	21.1	0	0.0	3.39	0.07
Withdrawal (comparison with before treatment)								
Increase in withdrawal symptoms of ≥100%	7	28.0	1	5.3	1	16.7	3.75	0.05
Increase in half or more of withdrawal symptoms	15	60.0	7	36.8	2	33.3	2.32	0.13

Relapse refers to a worsening of symptoms compared to the end of treatment. We defined relapse as any of the following changes since the end of the treatment study: 1) a 100% increase in anxiety symptoms, as rated on the Hamilton anxiety scale, 2) a 100% increase in the frequency of panic attacks, or 3) a decrease of 2 or more points on the global improvement scale. Rebound is a worsening of symptoms compared to baseline (before treatment). We defined rebound as 1) a 50% increase in anxiety, as measured with the Hamilton anxiety scale, compared to baseline, 2) a 100% increase in panic attacks compared to baseline, or 3) a global improvement scale rating of 3 or less (indicating symptoms worse than at baseline). Relapse or rebound was judged to have occurred if a subject met the stated criteria at any visit.

Using the withdrawal symptoms checklist, we identified symptoms that became worse during the taper and discontinuation of study medication than they had been at baseline. To do this, for each patient we subtracted the baseline value for each item, rated on a 4-point scale, from the highest value recorded during dose reduction or after discontinuation. We then calculated the group's mean change from baseline for each item and in this way identified 18 symptoms that became worse than they had been at baseline. The sum of the ratings for these 18 symptoms yielded a total withdrawal symptom score for each subject at each observation period. We defined withdrawal as 1) a 100% increase in the total withdrawal symptom score over the baseline score or 2) increases in the scores for half of the withdrawal symptoms compared to baseline.

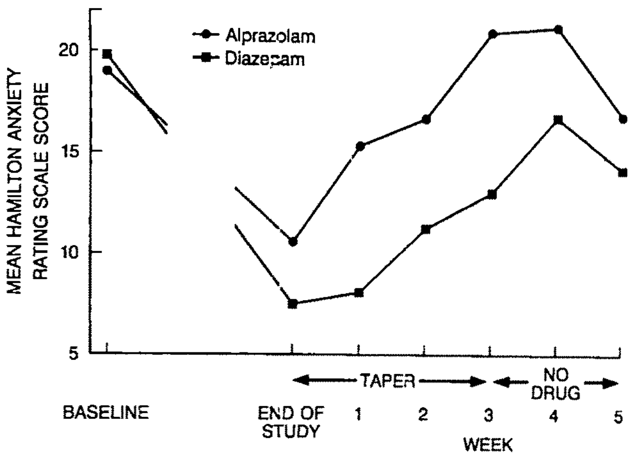
Comparisons of the subjects taking alprazolam and diazepam were made at the end of the treatment study, the last 3 weeks of dose reduction, and the first 2 weeks without medication. Because so few subjects were taking placebo, they were not included in most analyses. Analyses of variance for repeated measures were performed within treatment groups over time for anxiety and withdrawal symptoms. The starting point for these analyses was the end of the treatment study, and values for weeks 2, 3, and 4 of the discontinuation study were used to avoid observation periods with numerous missing values (weeks 1 and 5). Testing for Drug by Time interactions was done first, and, if none were found, drug and time main effects were examined. The frequencies of relapse, rebound, and withdrawal in the groups taking alprazolam and diazepam were compared by means of chi-square tests. The subjects who met the criteria for these outcomes at any observation period were included in the comparisons.

Finally, we examined baseline variables for predictors of anxiety and withdrawal symptoms during discontinuation. For this analysis we used the scores at the end of the last week of dose reduction. The relationships between baseline variables and those outcome measures were analyzed with stepwise multiple regression models.

RESULTS

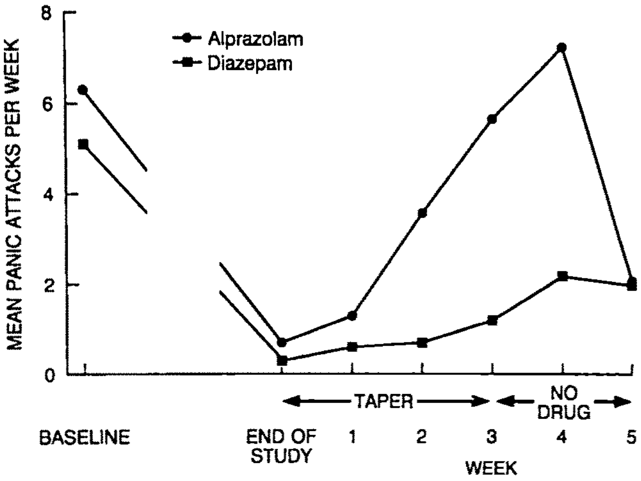
The discontinuation study (2 weeks without medication) was completed by 36.0% of the subjects taking alprazolam (N=9) and 42.1% of those taking diazepam (N=8) (χ^2=0.16, df=1, p=0.68) and by 66.7% of those taking placebo (N=4). Anxiety symptoms were rated as severe or extreme, at some point during the discontinuation, by 68.0% of the patients taking alprazolam (N=17) and 26.3% of the patients taking

FIGURE 1. Mean Hamilton Anxiety Ratings During Medication Discontinuation for Panic Disorder Patients Taking Alprazolam (N=25) or Diazepam (N=19)[a]



[a]Repeated measures analysis showed a significant time effect (F=12.75, df=3, 94, $p<0.0001$) but no significant drug effect (F=1.54, df=1, 42, p=0.22) or Drug by Time interaction (F=0.86, df=3, 94, p=0.46).

FIGURE 2. Mean Frequency of Panic Attacks During Medication Discontinuation for Panic Disorder Patients Taking Alprazolam (N=25) or Diazepam (N=19)[a]



[a]Repeated measures analysis showed a significant time effect (F=3.32, df=3, 94, p=0.02), a nearly significant drug effect (F=3.55, df=1, 42, p=0.06), and no Drug by Time interaction (F=0.89, df=3, 94, p=0.44).

diazepam (N=5) ($\chi^2=7.50$, df=1, p=0.006) and by 16.7% of those taking placebo (N=1). Similarly, 60.0% of the patients taking alprazolam (N=15) reported that, at some point, their anxiety symptoms became worse or much worse than they had been at baseline, compared to 26.3% of the patients taking diazepam (N=5) ($\chi^2=4.94$, df=1, p=0.03) and 16.7% of those taking placebo (N=1). Sixty percent of the subjects taking alprazolam (N=15) reported the development of new symptoms, as did 63.2% of the subjects taking diazepam (N=12) ($\chi^2=0.05$, df=1, p=0.83) and 33.3% of those taking placebo (N=2). Forty-eight percent of the patients taking alprazolam (N=12) made unplanned telephone contacts to report distress, compared to 26.3% of the patients taking diazepam (N=5) ($\chi^2=2.14$, df=1, p=0.14) and none of those taking placebo.

Table 1 shows the percentage of patients in each treatment group who met the criteria for relapse, rebound, and withdrawal. According to these figures, the majority of the subjects taking alprazolam and diazepam relapsed, and the rate differed little between them. Most of the patients who had stopped having panic attacks by the end of the treatment study began experiencing them again during the tapering or after discontinuation of drug treatment (73.7% of the subjects taking alprazolam and 60.0% of those taking diazepam). Fewer subjects met the criteria for rebound than for relapse, but the rate of rebound among the subjects taking alprazolam was more than double that among the subjects taking diazepam. Using the least stringent criteria (i.e., a 10% increase in the Hamilton anxiety scale score over baseline), we identified rebound in 68.0% of the alprazolam subjects and 36.8% of the diazepam subjects ($\chi^2=4.23$, df=1, p=0.04) and in 16.7% of the placebo subjects. Still fewer subjects met the criteria for withdrawal, but, again, a larger percentage of alprazolam subjects qualified.

Figure 1 shows the mean Hamilton anxiety scale scores during dose reduction and after discontinuation of alprazolam and diazepam treatment. The increase in anxiety began sooner and reached a peak earlier for the subjects taking alprazolam than it did for the subjects taking diazepam. The most intense anxiety was experienced during the last week of dose reduction or the first week without medication. Repeated measures analyses showed statistically significant drug and time effects for the global ratings of anxiety and global improvement but no significant drug effect for the Hamilton anxiety ratings. No significant Drug by Time interactions were observed with any of the measures. As can be seen in figure 1, the profiles of increasing anxiety symptoms appeared parallel for the subjects in the two groups. Figure 2 shows differences in the frequency of panic attacks for the subjects taking alprazolam and diazepam. A repeated measures analysis showed a significant time effect, a nearly significant drug effect, but no Drug by Time interaction. The frequency of attacks reached a peak at the end of the first week without drug in both groups of subjects.

Table 2 shows the 18 withdrawal symptoms that became worse during drug discontinuation than they had been at baseline. The mean increase and the percentage of subjects who reported worsening are presented for each symptom. The symptoms showing the greatest increases were decreased appetite, impaired coordination or balance, and increased sensitivity to light. The mean total withdrawal symptom scores

TABLE 2. Withdrawal Symptoms of 34 Panic Disorder Patients During Discontinuation of Alprazolam or Diazepam Treatment[a]

Symptom From Withdrawal Symptom Checklist	Increase in Score[b]		Patients Worse	
	Mean	SD	N	%
Decreased appetite	0.50	1.2	12	35.3
Impaired coordination or balance	0.44	1.4	12	35.3
Increased sensitivity to light	0.38	1.3	11	32.4
Initial insomnia	0.26	1.4	12	35.3
Trouble thinking clearly	0.26	1.4	13	38.2
Depressed mood	0.24	1.2	10	29.4
Dizziness or lightheadedness	0.24	1.4	10	29.4
Muscle aches or cramps	0.24	1.3	12	35.3
Decreased libido	0.21	1.2	8	23.5
Becoming upset easily	0.18	1.3	13	38.2
Fainting	0.18	0.9	8	23.5
Muscle weakness	0.15	1.1	8	23.5
Weight loss	0.15	1.0	6	17.6
Feelings of unreality	0.15	1.3	9	26.5
Impaired memory	0.15	1.4	13	38.2
Irritability	0.09	1.0	10	29.4
Depersonalization	0.09	1.1	7	20.6
Muscle twitching	0.03	1.0	6	17.6

[a] Baseline data were not obtained for 10 subjects.

[b] Items rated on 4-point scale; 0=absent, 3=severe. With the exception of the first three symptoms listed, the mean increases were not statistically significant ($p<0.05$).

(sum of scores for 18 symptoms) for the subjects taking alprazolam and diazepam were examined by means of a repeated measures analysis. This showed statistically significant time ($F=8.62$, $df=3, 94$, $p<0.0001$) and drug ($F=4.83$, $df=1, 42$, $p=0.04$) effects but no significant Drug by Time interaction ($F=0.66$, $df=3, 94$, $p=0.58$). The symptoms increased, peaked during the first week without medication, and during the second week without drug returned to the levels seen at the end of the treatment study. The subjects taking alprazolam experienced more severe withdrawal symptoms than did those taking diazepam.

We examined the influence of a series of baseline demographic and illness variables on the level of anxiety and withdrawal symptoms during drug discontinuation. Because we observed no important differences between the subjects taking alprazolam and diazepam, we combined the groups for this analysis. For outcome variables we selected the level of anxiety and withdrawal symptoms at the end of the last week of dose reduction. We also created models using the maximum anxiety and withdrawal symptom scores and the mean scores for the last 2 weeks of dose reduction and the first week without drug. Table 3 shows the baseline variables (dichotomized or trichotomized for the table) that were predictive of anxiety and withdrawal symptoms during the last week of dose reduction. A stepwise multiple regression analysis showed that the baseline score on the Self-Rated Anxiety Scale and drug were predictive of anxiety symptoms during the last week of dose reduction. Together these variables accounted for 48.1% of the variance. The level of anxiety and drug were also predictive of withdrawal symptoms during the last week, accounting for 40.1% of the variance.

TABLE 3. Relation of Baseline Variables to Anxiety and Withdrawal Symptoms During Discontinuation of Alprazolam or Diazepam in 44 Panic Disorder Patients

Baseline Variable	Level of Symptoms During Last Week of Dose Reduction			
	Hamilton Anxiety Rating		Withdrawal Symptom Score	
	Mean	SD	Mean	SD
Panic subtype				
Extensive avoidance	22.5	2.7	22.5	3.0
Limited avoidance	15.9	2.2	9.8	1.7
Uncomplicated	12.6[a]	4.3	9.6[a]	4.2
Major depression				
Present	22.1	2.0	13.5	2.0
Absent	15.0[b]	2.2	11.9	2.3
Personality disorder				
Present	22.1	3.1	17.1	3.3
Absent	13.6[b]	2.3	11.1	2.5
Duration of illness[c]				
Long	19.0	2.0	12.9	2.1
Short	16.3	2.3	12.2	2.5
Drug				
Alprazolam	21.1	2.1	16.4	2.1
Diazepam	13.1[d]	2.3	7.5[e]	2.1
Dose[c]				
High	19.7	2.0	14.7	1.9
Low	12.5[b]	2.6	7.4[b]	2.7
Hamilton anxiety rating[c]				
High	20.4	2.3	15.4	2.3
Low	13.2[b]	1.8	8.4[b]	1.8

[a] $p<0.10$, one-way ANOVA with pairwise follow-up.

[b] $p<0.05$, t test.

[c] Subjects grouped according to scores above and below the median.

[d] $p<0.02$, t test.

[e] $p<0.01$, t test.

DISCUSSION

We found, as have previous investigators, that the discontinuation of alprazolam treatment is associated with greater distress than is discontinuation of diazepam treatment. Alprazolam is a relatively short-acting drug with a half-life of 12 to 15 hours, whereas the half-life of diazepam is 15 to 90 hours (25, 26). Consequently, we would expect rebound anxiety and/or withdrawal symptoms to appear sooner with alprazolam than with diazepam and to be more severe initially. In fact, we observed a similar pattern of symptoms in the subjects taking alprazolam and diazepam, except that the increase appeared earlier for those discontinuing alprazolam treatment. This is not to say that the overall distress due to alprazolam discontinuation is greater; the difference may be that the symptoms develop sooner and are more intense but last for a shorter time. However, our findings suggest that shorter-acting benzodiazepines, such as alprazolam, may be associated with more intense rebound anxiety and/or withdrawal symptoms and that psychological dependence, reinforced by these phenomena, may occur more often as a consequence. This view is consistent with the limited data available on the subject (10, 11).

Our data suggest that reducing the dose of alprazolam by 0.5 mg every 3 days is too rapid for many patients who have been taking therapeutic doses for 6 months or more. Roughly two-thirds of our alprazolam patients experienced severe anxiety that was worse than the anxiety they had had before treatment began, and only about one-third were able to complete the discontinuation study (2 weeks without drug). The current manufacturer's guidelines call for tapering at a rate of no more than 0.5 mg every 3 days, but slower rates, such as 0.25 mg or even 0.125 mg every 3 days, should usually be employed, especially when the dose falls below 2 mg/day. Regardless of the rate at which the dose is tapered, adjustments should be made on an individual basis and steps should be taken, through the use of psychological and pharmacologic measures, to minimize the patient's discomfort (10). Even so, it is not clear whether slowing the rate reduces the overall distress or merely prolongs the period of distressing symptoms. This is an important issue that needs to be clarified.

The high relapse rate in this study is consistent with the chronic nature of panic disorder (2–8). All of our subjects had responded to long-term pharmacotherapy, and 70%–80% relapsed once they stopped taking medication. Although rebound anxiety had not had time to dissipate by the end of the study, it seems unlikely that time would have substantially altered the proportion who relapsed. This rate is consistent with other reported rates of relapse after discontinuation of treatment with benzodiazepines and other drugs used to treat anxiety disorders, although the literature on this question is limited (9, 18, 27–31, and unpublished data of D.V. Sheehan, 1986). The frequent occurrence of relapse means that some patients who receive substantial help from drugs may need to continue taking them indefinitely. In that case, the long-term risks and benefits of benzodiazepines and other drugs used for maintenance therapy become particularly important.

We were able to identify a group of symptoms that became worse when drug treatment was stopped than they had been at baseline. These symptoms appeared to be typical of benzodiazepine withdrawal, although they overlapped with anxiety symptoms (e.g., initial insomnia). The emergence of such symptoms suggests that at least some patients experienced a withdrawal syndrome in addition to more severe anxiety symptoms. Perhaps most distinctive were the unusual or distorted perceptions reported by five alprazolam patients and three diazepam patients. These included a feeling of movement when there was none and the perception that body parts had become separated from the rest of the body. Also reported were sensations of floating and falling, shimmering vision, and faulty depth perception. Certain authors have regarded such perceptual distortions as distinctive of benzodiazepine withdrawal (32).

We found that the level of anxiety symptoms at the time of enrollment in the treatment study was strongly predictive of relapse and rebound at the time of discontinuation. However, we also found that the drug (alprazolam versus diazepam) contributed to the variance in rebound and withdrawal. As previously stated, alprazolam was more often associated with rebound and withdrawal as defined in this study. These observations are consistent with our understanding of the differences between relapse, rebound, and withdrawal and with what is known about factors that influence the occurrence of benzodiazepine withdrawal phenomena. Thus, we found that relapse is more apt to occur in more severely ill patients, whereas rebound and withdrawal are more closely related to the half-life of the drug. In this study the effect of dose was largely eliminated by the use of a fixed rate of dose reduction, which allowed more time for stopping higher doses. Other important factors were duration of use and rate of discontinuation (10), but they were not examined in this study.

This discontinuation study has a number of limitations. Although it was double-blind and placebo-controlled, the patients were aware that their treatment was being discontinued, and this may have caused them to anticipate or exaggerate symptoms (33). Also, the study was limited by a large number of dropouts, a small number of subjects taking placebo, and a relatively short period of observation after drug treatment was stopped. Also, two factors may have contributed to more severe symptoms in the patients taking alprazolam. The first has to do with dose. Even if we assume that 1 mg of alprazolam is equivalent to 10 mg of diazepam—which may not be the case—the dose taken by the diazepam patients was slightly less than that taken by the alprazolam patients. The second factor has to do with selection. The patients who responded to alprazolam—and therefore participated in this discontinuation study—may have had more severe anxiety at baseline than those who responded to diazepam (34). However, there is not much evidence for this possibility aside from slight differences in the frequency of panic attacks and the extent of phobic avoidance at baseline.

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Suicide, Stressors, and the Life Cycle

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Objective: Relationships between stressors and suicide might be expected to vary with stages of the life cycle. The purpose of this study was to examine this possibility. Method: The authors examined the first 204 consecutive cases from the San Diego Suicide Study, a federally funded investigation of 283 suicides, for possible relationships between suicide and age and the frequency of specific stressors. Information was gathered from family members, spouses, acquaintances, employers, other witnesses, physicians, and other professionals by trained interviewers using a structured format. Hospital, physician, therapist, school, and police records were also included when available. DSM-III *diagnoses were made by consensus of two investigators. Life events information was also reviewed independently by the investigators to determine stressors (if any) for each case. Results: Of the 202 subjects for whom data were available, 195 (97%) had one or more stressors; 137 male subjects had a total of 272 stressors, and 58 female subjects had a total of 115 stressors. The authors found predictable patterns of the three most common stressor groups—conflict-separation-rejection, economic problems, and medical illness. The majority of the stressors among subjects 80 years old or older were illnesses. The only significant difference between the sexes was that more men than women had economic problems as a stressor. Conclusions: The variations in the patterns of stressors found in this study of suicides coincide with adult development theory. The lack of population comparison subjects and stressor scoring validation, however, limits the predictive value of these data in assessing suicidal persons.*

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Social factors as contributors to suicide have been a focus of research since at least the time of Morselli (1) and Durkheim (2). Systematic clinical studies of individual suicides (3, 4) have found psychosocial stressors in virtually every case. Relationships between specific life events or stressors and suicide have been described (5–7). Variations in stressor sensitivity have also been shown to occur among different psychiatric diagnostic groups (8, 9). Since it is thought that specific developmental tasks must be mastered during different life stages (10), relationships between stressors and suicide might also be expected to vary with stages of the life cycle. In this report, we examine the first 204 consecutive cases from the San Diego Suicide Study for possible relationships between suicide and age and the frequency of specific stressors.

METHOD

The San Diego Suicide Study is a federally funded investigation of 283 suicides. The first 204 consecutive cases of this study are the subjects of this report. The method of the entire study has been elaborated elsewhere (4). Information was gathered from family members, spouses, acquaintances, employers, other witnesses, physicians, and other professionals by trained interviewers using a structured format. Hospital, physician, therapist, school, and police records were also included when available. *DSM-III* diagnoses were made by consensus of two investigators. Life events information was also reviewed independently by the investigators to determine stressors (if any) for each case (11–13). The initial 26 types of stressors were condensed into the eight broad categories listed in table 1. Cases that had more than one stressor in any of the combined groups were counted only once for that group. Chi-square with Yates's correction was used to determine the significance

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TABLE 1. Frequency of 387 Stressors by Decade of Age Among 195 Suicides From the San Diego Suicide Study

	Age of Subjects (years)																	
	≤19 (N=9)		20–29 (N=84)		30–39 (N=86)		40–49 (N=46)		50–59 (N=72)		60–69 (N=40)		70–79 (N=27)		≥80 (N=23)		Total (N=387)	
Stress	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Conflict-separation-rejection	5	56	30	36	37	43	12	26	20	28	9	23	4	15	4	17	121	31
Economic problems	2	22	22	26	26	30	17	37	19	26	5	13	0	0	1	4	92	24
Medical illness	1	11	3	4	5	6	8	17	15	21	16	40	13	48	13	57	74	19
Death of significant other	0	0	5	6	5	6	2	4	6	8	3	8	4	15	2	9	27	7
Legal problems	0	0	13	16	8	9	1	2	2	3	2	5	0	0	0	0	26	7
Move	1	11	4	5	3	4	1	2	4	6	1	3	1	4	0	0	15	4
Illness of family member or significant other	0	0	1	1	0	0	2	4	2	3	3	8	4	15	0	0	12	3
Other	0	0	6	7	2	2	3	7	4	6	1	3	1	4	3	13	20	5

of differences. A probability of less than 0.05 was considered significant.

RESULTS

There were two cases (both male subjects) for which not enough information was available to assess stressors. Of the remaining 202 subjects, 195 (97%) had one or more stressors. The 137 male subjects had a total of 272 stressors, an average of 1.99 each, and the 58 female subjects had a total of 115 stressors, an average of 1.98 each.

Table 1 shows the frequency of stressors by decade of age for the 195 suicides for whom a stressor was identified. Conflict-separation-rejection was the most frequent group of stressors through the sixth decade and then appeared to decline gradually. Economic problems rose to a peak in the fifth decade and then fell to almost nothing in the eighth and ninth decades. Medical illness remained infrequent during the first four decades, then increased progressively until the majority of the stressors among subjects 80 years old or older were illnesses. The relatively small numbers of the remaining stressors made it difficult to discern patterns.

Economic problems were significantly more frequent among the stressors for male subjects (77 [28%] of 272) than among female subjects (15 [13%] of 115) (χ^2=9.57, df=1, p=0.002). This was the only significant difference between the sexes.

DISCUSSION

The variations in the patterns of stressors in these 202 cases of suicide coincide with adult development theory (14).

Interpersonal conflicts, separations, and rejections were the predominant stressors associated with the suicides in adolescence and early adulthood. Adolescents struggle to establish their own identity and separate from their parents. They are especially vulnerable to rejections from their peer group. By early adulthood, the support of school and adolescent peer groups may no longer be present. The danger of isolation is very real if lasting intimate relationships are not forged (10). Career choices are being made and implemented and might fail, and parental support may no longer be available (15). The rate of the conflict-separation-rejection stressor decreased from 56% among the suicides who were 19 years old or younger to 17% among those who were 80 years old and older. It is possible that separation issues become less disruptive as they recur throughout life.

Economic problems peaked as a stressor among the suicides who were 40–49 years old. By midlife, one is raising and educating children, while aging parents are becoming more dependent (14). As a result, the financial pressures on the middle-aged adult can be enormous. The male-to-female ratio of 2:1 for economic problems as a stressor among the suicides might be explained by the conjecture that, traditionally, men have more self-esteem tied up in financial success than women. It may also be that women are more often supported by men in this society than the reverse.

The frequency of illness as a stressor rose precipitously beginning in the 40–49-year-old age group. This might reflect an increased susceptibility to illness as a stressor due to the preoccupation with body image that occurs during the "midlife crisis" (14) For the older suicides, their own mortality and physical limitations may have become more apparent as they witnessed the death of friends and spouses. In the light of this, the relatively low rate of the death of a significant other as a stressor is somewhat surprising, particularly in the older groups. The low rates of this and the remaining stressors, however, make discernment of patterns by decade less easy.

Several factors make general clinical application of these data to suicide prediction and/or prevention problematic. The first and perhaps foremost is deciding post-mortem if an event that occurred was, in fact, stressful. There is no clear agreement on the distinction between presumably neutral life events and stressors. The complexity of this issue in medical research has been thoroughly reviewed (16). Debates continue over such elementary issues as how to weight various elements of an event (17) or even whether weighting is necessary (18).

This problem is exemplified by the seven cases of suicide in our study group who were judged not to have stressors. We were unable to identify any potentially negative circumstances for only one of these—a 16-year-old boy. The others were a 27-year-old woman with socioeconomic problems related to her substance abuse, a 33-year-old gay man on probation for substance abuse, a 36-year-old schizophrenic man who was decidedly unhappy about his illness, a 42-year-old man with domestic problems secondary to his drinking, a 48-year-old diabetic woman who thought, erroneously, that her illness was causing her family's financial problems, and an 84-year-old woman who was described as having a lifelong dissatisfaction with life in general. Although it could be argued that the problems of these six patients could have been included as stressors, their inclusion would not have changed the pattern of stressors in the study group. The question remains as to whether our decision to include the other stressors was, in fact, scientifically justified. Even if epidemiologic data were gathered demonstrating that life events (good or bad) are less common in the population in general than among suicides, the question of how to score such events in an active clinical situation requires further extensive validation studies.

Deciding when a stressor may have occurred is another important problem. For example, the timing of a particular stressor—interpersonal loss or conflict—has been shown to be a factor in suicide by alcoholics (8, 9). The validity of the determination of when the stressor occurred depends not only on the accuracy of informants but also on the specificity of the stressor. It is usually relatively easy to pinpoint the death of a spouse. Precisely when illness or financial problems began or when they became stressful is usually less clear. We chose to include events that were determined to be causing the subject stress at the time of death, regardless of when the event may have taken place. Determination of when the stress occurred in this study required consensus of two of the investigators and was based on the best available information. Overall, about 90% of the stressor events occurred within a year of death (9). Whether a year is too long or too short for either specific stressors or stressors in general to be related to suicide is not known. This is another example of a very complex issue that future studies must address in far greater detail.

It is possible, if not likely, that our list of stressors does not include events that will ultimately be determined to play a crucial role in unraveling the mystery of suicide. "Endogenous" factors that might alter vulnerability to suicide and be considered stressors may come to light as well. For example, it remains to be explained why, all else apparently being equal (which, of course, it never really is), white people in the United States have higher suicide rates than black people (with the exception of black men 20–25 years old). This is an almost imponderable difficulty. Obviously, therefore, future studies should not limit themselves to today's concepts of stress or lists of presumed stressors. Today's clinicians, however, must deal with what appear to be the facts now, no matter how limited the information.

Another important consideration not directly addressed here is the interaction of stressors with psychiatric illness. We have noted elsewhere (4) that psychiatric illness appears to be a necessary condition for suicide in the vast majority of cases. As already mentioned, we have also attempted elsewhere (9) to clarify one interaction—that between psychiatric diagnoses and stressors. Undoubtedly, many other interactions are important and need to be considered.

A fifth problem is a lack of data on comparison subjects in the population at large to confirm that these presumed stressors occur more frequently in suicides than in the population. Without such evidence, it could very well be argued that the patterns described here are coincidentally but not causally related to suicide. This seems counterintuitive, however. Human behavior is multidetermined, and the stress an individual experiences is likely to have at least some effect on suicidal behavior. We recognize that chronological, physiological, and psychological age are not necessarily synchronized. We also recognize that there may be critical periods, regardless of age, in each individual's life that may result in greater vulnerability to specific stressors. The observation that the stressors among our suicides follow predictable patterns based on adult development theory is unavoidable, however. We believe that future research into possible relationships between suicide and stress should somehow take age into account.

A final limitation is that because all our subjects were deceased we had to rely on secondary sources of information. Although we recognize the necessary limitations of any post-mortem study, we believe important leads for further investigation as well as helpful clinical clues can be explored by using such technically unconfirmable information. It is simply the best that can be done under the circumstances.

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Potential HIV Exposure in Psychiatrically Hospitalized Adolescent Girls

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The authors surveyed 23 psychiatrically hospitalized adolescent girls regarding behavior that involves high risk of HIV infection. Over half (57%) of the girls reported high-risk sexual activities; these girls were more likely to have sexually transmitted diseases, substantial drug abuse histories, and diagnoses of conduct disorder.

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Although adolescents account for just 1% of the reported cases of AIDS, the risk-related behavior of adolescents suggests that subgroups of teenagers are likely to become infected with HIV (1). Young adults aged 20–29 years account for 21% of the reported AIDS cases; the multiyear delay between infection and onset of symptoms implies that many AIDS cases among adults result from infections contracted during adolescence (1, 2). Evidence that heterosexual intercourse plays a larger role in HIV transmission in teenagers than in adults (1) suggests that adolescents may represent a significant conduit between currently infected and uninfected populations.

Only a few studies have examined HIV risk or infection in adult psychiatric patients (3, 4), and no published study, to our knowledge, has assessed risk-related behavior in adolescent psychiatric patients. Recognizing that a substantial fraction of our teenage inpatients were reporting preadmission behavior that entailed a high risk of becoming infected with HIV, we attempted to estimate the prevalence of AIDS-risk-related behavior among hospitalized female adolescents and to identify psychiatric subgroups who might be at especially high risk for HIV infection.

METHOD

As part of their routine gynecologic assessment, we obtained thorough sexual and substance abuse histories from all consenting adolescent girls hospitalized under our care at a state-funded, acute-to-long-term psychiatric facility in Ohio. Over the 5 months represented by this report, 33 adolescent girls (ages 12–17 years) were admitted. The girls described herein are all of the consenting adolescents who were hospitalized long enough to permit evaluation. Behavioral data were obtained from 25 girls by a female nurse practitioner using a structured interview derived from the AMA physician guidelines for HIV blood test counseling (5). Hospital policy precluded universal HIV testing, but consenting girls were examined for other sexually transmitted diseases as their symptoms and histories warranted. Socioeconomic status was not formally assessed, but most girls came from poor backgrounds and/or were in the custody of various agencies (e.g., county departments of human services).

Respect for confidentiality precluded our requesting explicit external corroboration of the girls' behavioral reports. In 24 cases, however, the girls' accounts were entirely consonant with information supplied to us by collaborative sources (parents, guardians, social agencies, etc.). We excluded from analysis the report of one psychotic girl whose description of her behavior was

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grossly at odds with the reports from all reliable external sources. We also excluded the report of one pregnant girl whose gynecologic and obstetric care was conducted at another treatment site.

For purposes of analysis, we assigned each girl to one of five drug use categories: I=no drug use (39%), II=rare to occasional use of alcohol and/or tobacco (17%), III=occasional use of legal and illegal drugs except cocaine (13%), IV=occasional use of illegal drugs including cocaine (13%), V=use of cocaine and daily use of at least one other drug (17%). Only one girl reported intravenous drug use; she was assigned to drug use group III. We classified at "high risk" for HIV infection any girl who reported having had more than six sexual partners during her lifetime, having had unprotected intercourse with a partner whose sexual history was unknown, or having had unprotected intercourse with someone who used intravenous drugs. The clinical diagnoses in this study were made according to the *DSM-III-R* criteria and were based on all information available to the treating psychiatrist at the time of discharge. Only one diagnosis—conduct disorder—occurred frequently enough to permit valid statistical evaluation.

RESULTS

Eighteen (78%) of 23 girls (mean±SD age=14.4±1.5 years, median age=14 years) reported that they had been sexually active. Of these 18, three (17%) stated that their partners had always used condoms. Thirteen (57%) of the 23 girls reported one or more sexual activities that put them at relatively high risk for HIV infection. Four girls (17%) had culture-proven sexually transmitted diseases (chlamydia, gonorrhea, and/or trichomonal infection). Eight girls (35%) received *DSM-III-R* diagnoses of conduct disorder; most of these had additional axis I diagnoses.

As table 1 indicates, level of drug use was significantly associated with multiple sexual partners, high-risk sexual activity, and sexually transmitted diseases, and it was marginally associated with a *DSM-III-R* diagnosis of conduct disorder. As expected, number of partners was significantly associated with sexually transmitted diseases and high-risk sexual behavior. Number of partners and level of drug use were negatively correlated with age; younger girls tended to report more sexual contacts and heavier drug use than older teens. We did not find a significant association between conduct disorder and high-risk sexual behavior (χ^2=2.6, df=1, p>0.1).

DISCUSSION

A majority of our female adolescent inpatients reported sexual activities that had placed them at high risk for exposure to HIV infection. In our patients, exposure risk was generally not a direct result of the patients' intravenous drug use but was incurred by means of unprotected heterosexual intercourse with individuals whose sexual or drug use histories were unknown.

TABLE 1. Relationship of Number of Sexual Partners and Drug Use to Sexually Transmitted Diseases, HIV-High-Risk Behavior, Conduct Disorder, and Age Among 23 Adolescent Girls in a Psychiatric Hospital

	Number of Sexual Partners		Level of Drug Use	
Test Variable	Test Statistic	p	Test Statistic	p
Positive culture for sexually transmitted disease	5.5[a]	<0.01	10.0[a]	0.02
Sexual behavior associated with high risk for HIV	10.5[a]	<0.002	14.5[a]	<0.002
Conduct disorder	28.5[a]	<0.05	33.5[a]	<0.10
Age	−0.50[b]	<0.02	−0.64[b]	0.001
Drug use group	0.87[b]	<0.001		

[a] Mann-Whitney U test, two-tailed p.
[b] Spearman's rho, two-tailed p.

Studies of adults have shown significant associations between HIV-risk behaviors and alcohol and cocaine abuse (unpublished data of A.J. Saxon and D.A. Calsyn, 1990, and J.C. Mahler et al., 1990). Within the 23 hospitalized adolescent girls that we evaluated there was a clustering of patients with high levels of drug abuse, numerous sexual partners, sexually transmitted disease, and conduct disorder. That a rather small survey group should yield significant associations among sexual activity, drug use, sexually transmitted diseases, and conduct disorder is surprising; that such associations should exist among adolescent inpatients is not. Two surveys of adolescents in the general population (6, 7) have revealed significant correlations between sexual activity and amount of drug use, and there is no reason to believe that psychiatric inpatients should prove exceptional in this regard. Our findings also are consonant with reports suggesting that genetic linkages may help explain the oft-noted aggregation of drug abuse, impulsive childhood temperament, and antisocial personality disorder in individuals and families (8).

In addition to suffering significant psychiatric comorbidity, our patients who reported sexual promiscuity or heavy substance abuse (particularly of cocaine) also were likely to have exposed themselves to infection with sexually transmitted diseases, including HIV. Unfortunately, experience suggests that these adolescents may be among those least likely to alter their behavior in response to information, admonitions, or educational programs. Clinicians and policy makers dealing with such teens should be aware that HIV infection and adult-onset AIDS may be among the significant health risks associated with childhood antisocial behavior and heavy substance abuse.

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Book Forum

Nancy C. Andreasen, M.D., Ph.D., Editor

MANIC-DEPRESSIVE ILLNESS: TWO VIEWS

Manic-Depressive Illness, *by Frederick K. Goodwin, M.D., and Kay Redfield Jamison, Ph.D. New York, Oxford University Press, 1990, 909 pp., $65.00.*

This masterpiece is in some respects an un-American book. During the past decades, the rapid pace of science in the United States has made technical reports—published in prestigious journals—the major vehicle of communicating scientific advances. Indeed, many books published today in the United States are expanded versions of scientific journals. At best, scientific advances have led to major technical breakthroughs; at worst, science has been reduced to a mindless gathering of masses of data. Psychiatry, which joined this technical thrust in the 1980s, appears to have taken a particularly unfavorable position regarding theoretical treatises on clinical syndromes. The Goodwin-Jamison book, which is the outcome of more than 10 years of scholarly labor in developing a coherent psychobiological perspective on manic-depressive illness, represents a repudiation of a positivist zeal that had gone too far. The book also illustrates how psychiatry can be at its best—both scientifically and aesthetically compelling. This achievement is all the more impressive in view of the fact that Dr. Goodwin is one of the most cited authors in the field of biomedical science and the fact that he wrote this treatise while running the world's largest agency conducting research on mental and addictive disorders.

Manic-Depressive Illness is a monumental achievement, not just in the magnitude of the effort but particularly in its scope and vision. It is descriptive, phenomenological, and clinical; historical and modern; methodological and integrative; psychological, biological, and psychobiological; pathophysiological and therapeutic; psychopharmacological and psychotherapeutic. Furthermore, it considers manic-depressive illness in its broader context—in relation to its social liabilities and virtues, its interface with alcohol and substance abuse, and its possible role in leadership and artistic creativity. The authors' perspective derives from their experience as psychopathologists, clinicians, and researchers—and as intellectuals—and serves as a role model for psychiatrists and psychologists.

The book represents a triumph of the medical approach to mood disorders, examined compassionately from the perspective of patients and based on objective and longitudinal observations of clinicians as well as on practitioners' integration of the yet imperfect—but often miraculous—psychopharmacological and psychosocial modalities of intervention.

Clinically, *Manic-Depressive Illness* is not only about bipolar disorder but also about the entire spectrum of recurrent mood disorders in the Kraepelinian sense, in their psychotic as well as temperamental variants. Without question, this is the best book on manic-depressive illness since Kraepelin's treatise on the subject.

Although uncharacteristic of books published in the United States, this treatise nevertheless illustrates what America can do at its best: surpassing the insights and visions it has borrowed from Europe—and other continents—and integrating them into a new order that is at the same time profound and relevant, elegant yet useful.

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Manic-Depressive Illness, *by Frederick K. Goodwin, M.D., and Kay Redfield Jamison, Ph.D. New York, Oxford University Press, 1990, 909 pp., $65.00.*

This book is beyond doubt the most authoritative text on this subject yet to appear. In a number of respects the book is outstanding: it is comprehensive (with more than 900 pages and 4,000 references) and broad in coverage, it is both systematic in its analysis of research findings and illuminating in its presentation of case material, and it gives a critical and informed overview of the range of information that is relevant to this important class of diseases. Most impressive of all, this compendium of meticulously presented information is (with the exception of a characteristically lucid chapter by Elliot Gershon on genetics) the work of the two authors. In this lies its strength. This is not merely a collection of research material. It is the presentation of the authors' synthesis of the literature in the light of their own experience of all aspects of the problem. It represents a remarkable and impressive achievement.

The volume consists of five sections: Clinical Description and Diagnosis, Clinical Studies, Psychological Studies, Pathophysiology, and Treatment. "The clinical reality of manic-depressive illness is . . . far more complex than the preferred term of the day, *bipolar affective disorder,* might suggest" (p. 55) is the appropriate conclusion to the chapter "Clinical Description." This and subsequent chapters do much to document the variety of manic-depressive illness. The evolution of the bipolar-unipolar concept is followed from Aretaeus of Cappadocia through to Falret, Baillarger, and their twentieth-century descendants Leonhard, Angst, Perris, and others. In defining the scope of their own work, Goodwin and Jamison write that "we became more and more convinced that isolating bipolar illness from other major depressive disorders prejudges the relationships between bipolar and unipolar illness and diminishes appreciation of the fundamental importance of recurrence" (pp. 4–5). For this reason they have adopted a Kraepelinian concept that includes recurrent major affective illness with and without mania, albeit with a particular emphasis on the bipolar form. In their chapter "Diagnosis," the authors draw attention to the overlap with the schizoaffective psychoses and to debate in which the Kraepelinian two-entities tradition is challenged by the concept of a psychotic continuum (pp. 101–103). Here as elsewhere the discussion is informed by a broad perspective on the recent and historical literature and eschews dogma.

The section on Clinical Studies includes chapters reviewing course and outcome, epidemiology (including social class and seasonality), the manifestations of the illness in childhood and adolescence, the relationship with alcoholism and drug abuse, and suicide. Of particular note in part three (Psychological Studies) are chapter 11, "Thought Disorder, Perception, and Cognition," and chapter 14, "Manic-Depressive Illness, Creativity, and Leadership." The former draws attention to the consistency of the finding of right (nondominant) hemispheric disturbance in affective illness, which provokes the question of whether this finding is a clue to the nature of the genetic contribution. The chapter on creativity and leadership represents the fullest and most compelling exposition of the case (developed for some time by Kay Jamison) that there is a relationship between the disposition to affective illness and high achievement in a surprisingly wide range of fields of artistic, spiritual, and political endeavor. This chapter on its own justifies a wide readership for the book.

We look to the section on Pathophysiology for illumination of the way ahead. What do we really know about the origins of the illness? Elliot Gershon emphasizes the force of the evidence for a genetic factor and the promise, as yet unfulfilled, of molecular genetics. He also does not shrink from some large unsolved problems, such as the limits of the phenotype and the apparent secular change in rates of illness in recent studies. In further chapters Goodwin and Jamison give a comprehensive account of the wide range of biochemical and pharmacological and endocrinological studies, the clinical correlates of the abnormalities that have been detected, anatomical investigations, and the importance of disturbances of sleep and biological rhythms. In chapter 20, a critical evaluation of the findings on pathophysiology assesses their significance and attempts to chart the way ahead. The authors wrestle with diverse aspects of the problem—the status of the monoamine hypothesis, the nature of the genetic contribution, and the meaning of sleep disturbance and periodicity of the illness—but do not pretend that an easy synthesis can be achieved. Any researcher with an interest in the fundamental mechanisms of affective disturbance would do well to consider the discussion here.

Part five, Treatment, gives a clinically based overview of efficacy with reference to long-term outcome and maintenance and with a particular emphasis on the evidence for the value of lithium and tricyclic antidepressants in prophylaxis of bipolar illness. Although they give appropriate weight to controlled trials, the authors also discuss the efficacy of anticonvulsants and other adjunctive medications, and there are useful and practical chapters on the role of psychotherapy and medication compliance as well as treatment of concomitant alcohol and drug abuse and the management of suicidal patients.

In summary, this is a thoughtful and well-informed presentation of what is known about manic-depressive illness. It is comprehensive with respect to research findings but at many points directly relevant to clinical practice. It is a book that all psychiatric libraries, all researchers on affective illness, and many clinicians will wish to acquire.

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SOMA AND PSYCHE

Emotion: A Reconsideration of the Somatic Theory, *by A.C. Papanicolaou. New York, Gordon and Breach, 1989, 142 pp., $35.00; $19.00 (paper).*

As computers draw ever nearer to demonstrating human-level intelligence, questions regarding the nature of emotion acquire new importance. It seems somehow obvious that no matter how intelligent the computer can become, its cognition will remain "cold," i.e., lacking in emotion. Perhaps a greater understanding of feeling states will provide important clues regarding the uniqueness of human mental processes.

With this question in mind, I eagerly delved into this book. A.C. Papanicolaou is Director of the Human Electrophysiology and Neuromagnetism Laboratory of the University of Texas Medical Branch at Galveston and, moreover, has an enduring interest in epistemology. Therefore, he is well-suited to shed light on the psychological, physiological, and philosophical nature of emotion.

The author begins with a review of William James's century-old theory, which states, first, that human emotions or, more precisely, the distinct quality of feelings consists in the perception of somatic, notably visceral, changes and, second, that the distinct differences in quality among different emotions derives from different patterns of somatic and visceral activation. Fear may be described as the sensation of a pounding heart and a sinking feeling in the gut. Other feelings have other distinctive somatic and visceral qualities—for instance, passionate desire, according to Papanicolaou, is felt as a kind of visceral pang that somehow is like the pang of hunger accompanied by autonomic changes involving the sex organs. This perspective assumes that different combinations of somatic sensations yield the vast coloration of our emotional life.

The remainder of the book is devoted to defending this theory against a long line of detractors. For example, early studies by Sherrington of animal viscera surgically separated from the CNS revealed that these animals continued to demonstrate a full range of emotional responses. Later animal studies demonstrated that lesions in or stimulation of specific subcortical regions interrupted or precipitated certain emotions. These findings also seem to contradict James's theory. In a well-known study, Schachter and Singer injected different subjects with stimulant medication in experiential fear-producing or mirth-producing contexts. The subjects experienced emotion according to context, suggesting that the somatic experiences induced by the drug produced something akin to general arousal but derived their specific qualities from alternative cognitive "sets" rather than from differing patterns of visceral sensation.

The author wards off these attacks on the so-called somatic theory of emotion by an extended display of intellectual parry and thrust. Surely none of these detracting experiments were absolutely definitive. A surgically treated animal that continues to behave in an angry fashion may not actually be experiencing anger; it may be that the anger-producing stimulus induces a brain process which in turn yields a skeletal response characteristic of this emotion, all in the absence of something akin to a conscious feeling. Schachter and Singer did not rule out the possibility that different experimentally induced affective states actually may have induced different and specific visceral responses over and above the common drug-induced effect. The fact that subcortical lesions of various sorts interrupt certain kinds of emotions by no means rules out the possibility that somatic sensation is necessary for an emotion to be consciously felt; analogously, the fact that an occipital lobe alone can induce "cortical blindness" by no means demonstrates that vision does not derive from the retina.

For better or worse, this book dwells a great deal on the phenomenology of emotion and assumes that much can be learned by introspective processes. Frequently the author appeals to the idea that emotions are somatically derived because that is how they feel. To his credit, he generally includes the caveat that introspection alone cannot rule out the possibility that this feeling is an illusion analogous to the experience of a phantom limb—one thinks the sensation is in one's body but it is really only in one's head. He also makes introspectively based appeals for a differentiation of skeletal and visceral sensations and for the idea that emotion accrues more from the latter than the former.

There is unfortunately no discussion regarding any empirical evidence that we human beings are able with great nuance to sense the state of our viscera. The author appeals to empirical studies that differentiate anger from fear on the basis of contrasting profiles of autonomically controlled events. For instance, studies have demonstrated that during anger the lining of the stomach becomes red and that this is accompanied by increasing peristalsis but that during fear the stomach lining becomes pale and that this is accompanied by decreased peristalsis. In either case there is no evidence, as far as I know, that we directly experience these visceral changes.

I was surprised that there was no discussion of the important work of Gary Schwartz and colleagues demonstrating that different emotions are accompanied by subtle but specific facial muscle activation as reflected in EMG changes, even when there is no visible change in the subject's facial expression. This makes a great deal of sense because an important function of emotion is social; facially expressed emotion is a very effective way for all social animals, including humans, to communicate happiness, distress, etc. These communications have great value for both the individual and the social group. I was also surprised that the author did not discuss in any detail the growing body of evidence demonstrating that emotional tone can have important effects on cognition and memory access. This literature seems important in further clarifying the relationship between "cerebrocentric" cognition and emotional processes and may have much to say regarding the "value" of emotional states from an evolutionary perspective.

All in all, whether emotions derive their sensate qualities in part or entirely from actual visceral sensation or these bodily feelings are an illusion seems a bit pedantic to me. Surely a great deal goes on somatically during emotional states; to what degree this activity is cause or effect cannot be answered by introspection and even seems quite removed from empirical study. The only data that directly address the direction of causality noted in this book are a study by Hohmann, reviewed in chapter six, which suggests that patients with spinal cord injuries—and impaired afferent projections from visceral organs and skeletal muscle—report less feeling than normal subjects. The design limitations of this study are substantial, and the findings are challenged by my own personal experience of persons with spinal cord injuries, who can positively overflow with all kinds of emotion.

Perhaps the book does offer an answer to my initial question—computers will never experience emotions because they do not have feeling, sensing bodies. Certain matters of psychiatric relevance are also clarified by this book. For one, we should not think of particular emotions as having one-to-one relationships with particular brain centers. This fact is driven home by the simple fact that we generally do not have simple emotions. Yes, there are anxiety, fear, sadness, and anger and, perhaps, brain centers for each. But what about whimsy, contentiousness, wistful longing, and all of the other emotions that color our human lives? Surely there is not a brain center for each. Finally, we still must come to grips with a central challenge for psychiatry: what is the relationship between normal emotion and pathological emotion? At issue may not be the question of where emotions come from but, rather, the tendency of certain individuals to "get stuck" in an emotion. The brain processes of the person experiencing anxiety or sadness from a reasonable cause may be physiologically indistinguishable from those of the individual with anxiety disorder or depression However, the former readily "recovers" from the anger or sadness and the latter does not. The question then becomes not only how we achieve the vast spectrum of emotions that color our lives but also how, in health, we so readily move from one emotion to the next while retaining a coherent and continuous sense of ourselves and the world.

In any case, I recommend this book for those with a special interest in the study of emotion or in phenomenological-introspective studies of mental processes in general.

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Health and Behavior: Selected Perspectives, *edited by David A. Hamburg and Norman Sartorius. New York, Cambridge University Press, 1989, 219 pp., $59.50.*

An individual's personal behavior is an important variable in modifying the processes of health and disease. This small volume, an outgrowth of the World Health Organization's program on biobehavioral sciences, reviews such interrelationships. Its contributors are international experts on a variety of public health issues that link physical health and social and behavioral disorders.

Drs. Hafner and Welz contribute a fine introduction about psychiatric epidemiology. Both the strengths and weaknesses of the case register method, field and community studies, and the use of general practice data are reviewed to provide a succinct overview. The discussion of cultural influences on mental health suggests that sociocultural factors are only minimally connected with schizophrenia. Suicidal behavior, however, varies depending on cultural influences. Unfortunately, the chapter on suicidal behavior was submitted before the Epidemiologic Catchment Area data (1) were available. Furthermore, it does not discuss more recent data suggesting that the incidence of schizophrenia may be declining (2).

"Food Related Behavior" by Drs. Abdussalam, Foster, and Kaferstein discusses the relationships between behavior and culture and technology. Health beliefs and idiosyncratic ideas regarding food contribute to nutritional defects in many cultures. The authors emphasize that food is a cultural concept but that nutrient is a biological variable. They remind the clinician of the value of understanding the idiosyncratic health beliefs of individuals as they affect the patient's seeking treatment as well as the patient's actual dietary habits.

Two chapters are devoted to children. Theodore Wacks documents the importance of the psychosocial environment in children's acquisition of developmental skills. A comprehensive bibliography complements this chapter. Philip Graham, an eminent British child psychiatrist, reviews "Children in Danger" from biological stresses such as malnutrition as well as from sociocultural stresses such as family disruption. Throughout the book, a global perspective is emphasized. The importance of child and adolescent psychiatry is underscored by the large percentage of the total population that children and adolescents represent. In 1980, more than 40% of the total population of many Central and South American countries were represented by children under the age of 15, in contrast to the United States, where only 23% of the population were children and adolescents.

Beatrix Hamburg reviews adolescent health care and disease prevention, focusing particularly on adolescent pregnancy. The authors of this book do not focus on alcohol and drug abuse, suggesting the international view.

Drs. Hafner and Welz pay attention to the elderly patient, emphasizing the role of increasing stresses and losses in the development of psychopathology in the elderly. These authors used international databases and cite studies from both Europe and the United States.

Prof. David Goldberg reviews the mental health aspects of general health care in an elegant and comprehensive manner, citing his own studies as well as many from the United States. He emphasizes the problem of the somatizing patient who takes up an inordinate amount of health care time in a variety of clinical settings. The references, again, are wonderful sources for further study.

The book concludes with three chapters. The first reviews the sociology of health care in developing countries, the second reviews the role of population movement and its effects on human health, and the third is a summary chapter providing a global perspective of the relationship between health and behavior.

The book is beautifully written and adds a unique perspective to the news that we read daily about epidemics, mass starvation, and forced migrations of large numbers of people. It emphasizes the role that psychiatry can play in understanding the effects of such trauma on behavior, and it also offers the reader a fine introduction to public health perspectives that demand psychiatric expertise. It is a useful resource volume that should be in all medical libraries.

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Psychiatric Consultation in Childbirth Settings: Parent- and Child-Oriented Approaches, *edited by Richard L. Cohen. New York, Plenum, 1988, 282 pp., $39.50.*

I read this volume with fascination because Dr. Cohen has been working for many years in the area of pregnancy-related psychiatric illness, a field I have also been working in for 15 years. Most of the chapters in this book were written by Dr. Cohen or his colleagues at Pittsburgh, but there are invited chapters: "Neonatal Intensive Care" by Klaus Minde and Donna Stewart from Toronto, "Genetic Counseling" by Ann Walker and Anne Spencer of the University of California, Los Angeles, and "Psychiatric Consequences of the New Methods of Conception" by Margaret Jensvold of the National Institute of Mental Health. Dr. Cohen obviously has a flourishing consultation-liaison service in a maternity hospital, and the core of this book is his account of the psychological adaptation to pregnancy (chapter five), his ideas on the classification of psychological disturbances (chapter six), and his exposition and management of clinical situations referred by obstetricians (chapter nine). Dr. Cohen has evidently developed a comprehensive semistructured interview exploring the personal history, psychodynamics, and adaptation of women in the antenatal period; some of the probes in this questionnaire are very interesting. Furthermore, Dr. Cohen is a widely read man, and this volume is a valuable source and entree into the literature.

In addition to Dr. Cohen's contributions, there is a thorough analysis of the use of psychotropic drugs and the effects of addiction in pregnancy and the postpartum period, there are the invited chapters already mentioned, and there is a chapter on the law concerning the rights of the mother and of the child. A good deal of thought is also given to the psychological effects of alternative birth centers compared with hospital deliveries in the university centers.

I do not wish to emphasize the defects of this valuable contribution because they stem from the problems of health care delivery in the United States. Dr. Cohen's practice seems to have been somewhat slanted toward the middle classes, and some of the patients referred to him would seem to British psychiatrists to be subclinical. There is comparatively little in this volume dealing with those conditions which we spend most of our time treating—puerperal psychosis, chronic postnatal depression in socially deprived mothers, and severe disturbances of the mother-infant relationship. To give an example, in chapter five there is a fascinating analysis of the stages of acceptance of pregnancy, which mentions several women who presented with "abdominal tumors" for which they requested surgery; however, there is no mention of the problem of neonaticide in women who come to term without ever recognizing that they are pregnant. The handicaps under which U.S. psychiatrists are operating are also well illustrated by the case history of a severely ill woman who discharged herself from the hospital expressing suicidal and homicidal wishes, including threats to kill the baby; all that could be done was to urge the staff from the community health clinic to contact the patient and to discuss the possibility of a home visit. In Great Britain a member of the psychiatric service (in some centers the specialized service for pregnancy-related psychiatric disorders), with the previous agreement of the general practitioner, would have been at her house within hours.

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Psychosomatic Medicine: Theory, Physiology, and Practice, vol. 1, *edited by Stanley Cheren, M.D. Madison, Conn., International Universities Press, 1989, 424 pp., $40.00.*

Psychosomatic Medicine: Theory, Physiology, and Practice, vol. 2, *edited by Stanley Cheren, M.D. Madison, Conn., International Universities Press, 1989, 553 pp., $40.00.*

Illness and disease can be viewed as adaptive failures at many levels of biological organization from both physiological and psychological perspectives. This long-awaited two-volume text presents the most up-to-date and relevant information on our current understanding of these failures as well as the ways in which individuals cope with these experiences. My fear on first reading it was that the 7-year gestation, brought about by realities quite beyond the ability of the editor to control, might result in a product 7 years out-of-date. On the contrary, some of the material is so fresh and stimulating that it was well ahead of its time when written. The chapter by Levine and Coe on endocrine regulation, for example, is one of the finest expositions on the subject I have ever read. This is only one of the outstanding parts of a comprehensive, focused, and scholarly publication that does credit to the authors and the editor.

The text is organized around three aspects of current psychosomatic medicine—psychodynamic psychiatry, psychophysiological research, and biobehavioral intervention. It attempts to put together under one umbrella the diverging and at times conflicting endeavors without diluting the contributions of any one point of view. The text begins with a section on Theoretical Considerations that moves from the general to the more focused. Weiner and Fawzy make an eloquent case for their integrative model, which attempts to account for the multiple factors—genetic, immunological, bacterial, nutritional, developmental, social, behavioral, and psychological—that protect against and predispose to initiate, maintain, and complicate the natural history of illness and disease. Other authors describe how psychosomatic concepts have developed and predict the directions of the future. Key concepts, including life-change stress and psychological vulnerability, are covered as well. The second section, Psychophysiological Research, is very rich and well-documented, with compelling research findings. The third section, Psychosomatic Illnesses and Processes, covers gastrointestinal, bronchial, connective tissue, myocardial, endocrine, and eating disorders. The fourth section focuses on Psychodynamic Treatment Approaches.

In reviews of this type of work one is always tempted to make comparisons with other works purporting to be on the same subject. For example, one of the widest selling texts in this field in Europe is also entitled *Psychosomatic Medicine* (1). That work is encyclopedic, massive, and very different from the object of this review. Yet it is strangely reminiscent of the works of the past. It lacks the comprehensive and integrative perspective of the psychosomatic model so carefully illustrated in Cheren's volumes. Although Cheren could be faulted for not putting more of his own considerable scholarship into the book and for not providing more tangible bridging from chapter to chapter, what comes across to me, and I suspect to many nonpsychiatrist physicians and student readers, is his belief that reductionism in medicine is dead and that the future will behold the emergence of a scientific psychosomatic approach to research and treatment in all of medicine.

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Hemispheric Specialization and Psychological Function, *by John L. Bradshaw. New York, John Wiley & Sons, 1989, 211 pp., $49.95.*

This book provides a scholarly overview of lateralization, primarily of hemispheric specialization, but in its wide-ranging approach, it also includes a discussion of the attack pattern of trilobite predators on the origin of organic chirality (why we are made up of L-amino acids and D-sugars). It critically reviews the literature on asymmetries of hemispheric function obtained from studies of neuroanatomy, clinical lesions, commissurotomies, and normal subjects. It also covers the origins of tool-making and language, the inheritance of handedness, and the interactions of gender and cognitive asymmetries. Using the information presented, the author summarizes and critically assesses the validity of numerous theories regarding the etiology, inheritance, and potential significance of these asymmetries, from Jaynes's theory of the origin of consciousness due to communication between the hemispheres (mentioned primarily to be discounted) to Geschwind and Galaburda's attempt to link testosterone to right-hemispheric embryogenesis and immune dysfunction.

This book will not be of pressing interest to most psychiatrists because it has almost nothing to say about psychiatric disorders in which issues of lateralization have been raised, such as schizophrenia, affective disorders, and hysteria. One of the few references to schizophrenia mentions that it is associated with overactivation of the left hemisphere, higher dopamine levels in the left hemisphere, and a tendency to turn to the right. Unfortunately, these conclusions are not referenced, so the evidence for them cannot be reviewed. My own understanding is that these conclusions are not correct. Bracha reported left-sided turning in drug-naive schizophrenic subjects. Posner, Flor-Henry, and Rotkin each found right-sided neglect, and higher levels of dopamine in the right hemisphere have been demonstrated by single photon emission computed tomography. I would have enjoyed a discussion by Bradshaw of these apparently contradictory claims, which are no more confusing than many in other areas of lateralization.

Less directly related to psychiatry is the perspective of the author on the popular applications of theories of lateralization. Theories about left- and right-handedness and hemispheric specialization have been used over the years to justify educational and therapeutic interventions. For example, after Broca's discovery there was a cult of "ambidexterity" that attempted to double children's brain capacity by training them to use both hands equally. In the 1930s, ambidexterity was blamed for causing dyslexia and stuttering, and efforts were made to promote right-handedness. Today, of course, our era promotes the virtues of the right hemisphere, the source of creativity and intuition, and educational exercises attempt to enhance its development.

In summary, this book amply demonstrates the complexity of this field and raises serious objections to the simplistic conclusions of pop psychology. It is an excellent resource for the psychiatrist. However, it is hard to imagine that such an exhaustive review of this potentially overstudied field will be become a psychiatric bestseller.

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PAIN

Coping With Chronic Pain: A Guide to Patient Self-Management, *by Richard W. Hanson, Ph.D., and Kenneth E. Gerber, Ph.D. New York, Guilford Press, 1990, 232 pp., $30.00.*

The authors of this book are clinical psychologists involved in teaching and research in behavioral medicine at the University of California. Their book consists of nine chapters: "Introduction," "Models of Pain," "Self-Management Training," "Self-Management of Physical Activities," "Coping With Pain Through Distraction," "Coping With Episodes of Intense Pain," "Managing Stress and Depression," "Organization and Management of a Chronic Pain Program," and "Beyond Self-Management Training."

The authors refer to the current "mechanistic" domination of medicine. They use low back pain to illustrate how the sufferer is a passive victim whose pain is to be eliminated by the expert with the use of technological instruments. The system of financial reimbursements for medical services leads to excessive use of medical procedures despite confusions in diagnosis and a 1% success rate in disk surgery. This, they claim, necessitates the development of self-management by patients to cope with chronic pain.

The scientific study of health care is determined by the model of pain chosen. The biomedical model is effective for acute conditions, but for chronic states the biopsychosocial model is useful because it focuses on the whole person. Although there are cognitive and emotional effects on sensory input, the authors say they are often ignored by medical practitioners. In the authors' program, which consists of lectures and group discussions, the biopsychosocial model is emphasized, no "cure" is offered, and the search for medical relief is discouraged. Admission of patients to the program is restricted to those who manage pain without a physician, who stop taking narcotics, and who cooperate fully. The authors say that although the physician has failed, "care is taken to avoid global condemnation of the medical profession."

Appropriate exercise is encouraged, contrary to traditional medical approaches, which, they say, "often" discourage activity. Disability is due to deconditioning, drugs, and iatrogenic fears. Living a full productive life despite physical impairment is encouraged. Cognitive, emotional, and behavioral features are taught for coping with and distracting oneself from pain. To cope with intense pain, situational triggers are to be found, and "as-needed" orders for analgesics, use of narcotics, excessive alcohol use, and hospital emergency room visits are to be avoided. To manage stress and depression, the influence of thoughts on emotion and behavior is applied to find reasonable solutions. Patients with psychiatric problems are referred for individual therapy.

Ideally, the authors say the program should be conducted away from a hospital because being in the hospital may renew interest in medical treatment. Patients are discharged if they fail to observe 10 strict rules. The program lasts 3–4 weeks, inpatient attendance is preferred, only 8% do not finish, and 100 inpatients are accommodated yearly. A physician decides who is not suitable for medical care for pain. The authors describe this physician as one who "achieves professional satisfaction in interactions with patients that are devoid of many of the traditional treatment procedures in which the physician has been trained."

Several detailed case reports are presented of patients who were not well-suited for the program even though psychosocial factors were present. Nevertheless, the authors believe that "all people [must] assume greater personal responsibility for managing their own health rather than placing all responsibility onto the medical care system." To avoid pain therapy failures, clinicians should be aware of and practice the multidisciplinary approach.

The authors are involved in a courageous attempt to help the sufferer for whom medicine allegedly can do nothing. But it is not convincing. That the authors were "impressed" with the results is not enough. Their findings were not exposed to statistical evaluation with controls, patients were highly selected, physical diagnoses were unclear, and psychiatric diagnoses were absent.

The biopsychosocial model is not new. It has been applied by this name and others by many medical practitioners. The authors' criticisms of medicine are frequently naive. Quotes to support their attitudes are selected with bias, and one asks whether the medical resources were exhaustively used by those who were considered "medical failures." The 3–4-week program seems to be dependent on expectations and personal attention for success. (Nothing is mentioned about spontaneous remissions in chronic disease.) I felt a note of coercion for desperate candidates. There is danger in discouraging a reasonable awareness of pain. A patient with one painful condition may develop another illness, and there is progress in medicine. For example, according to a personal communication from John S. Train, interventional radiology was effective in finding a correctable lesion in one patient who had suffered 6 years of bleeding with repeated attempts at relief.

In my opinion, the program described by the authors is regressive, and their book would have been better if they had included an internist and a psychiatrist as coauthors.

The relationship between emotional stress and biological illness is receiving more and more attention in both research and bedside practice. This book attempts to deal with this serious and provocative problem. It is well organized and well written although in parts repetitious and wordy and provides an interesting review of biosocial factors in medical practice. Except for its critical references to medicine, it may be recommended for inexperienced mental health clinicians. The book contains a sizable bibliography and a workable index.

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ETHICS, LAW, AND RELIGION

Medical Ethics for Physicians-in-Training, *by Jay E. Kantor, Ph.D. New York, Plenum, 1989, 219 pp., $29.95.*

Defining ethics as the study of how people ought to act, Dr. Kantor has set out to translate his experience in dealing with ethical problems in clinical settings into a guide for physicians and medical students on how they ought to act when confronted with ethical choices. His book is not intended to be comprehensive but, rather, to deal with common and recurrent concerns. Dr. Kantor tells us that neither the law nor ethical codes will adequately resolve moral issues; these must be addressed through an understanding of ethical principles and their application. Rejecting answers based on ethical cultural relativism and self-interest, he outlines the tenets and implications of the four major philosophical theories that purport to give direction to the ethical decision maker. These are utilitarianism, Kantian autonomy, natural law, and social contract (Hobbes to Rawls). The description of these theories for a general medical audience is cogent and informative. Dr. Kantor acknowledges that it may be easier said than done to apply a principle to the staggering ethical dilemmas of real life, but he is hopeful that clear reasoning and additional facts may resolve the issue. (He evidently at least partially rejects the dictum that one cannot derive "oughtness" from "isness.") When issues remain unresolved, one should not resort to situation ethics but adhere consistently to a particular theory. He makes it clear that his own preference is for autonomy approaches, a bias whose influence on some of his judgments can be seen throughout the book.

The titles of the remaining chapters—"Informed Consent and the Right to Refuse Treatment," "Personhood and the Right to Life," "Euthanasia, Confidentiality, and Psychiatric Ethics"—indicate the areas that Dr. Kantor regards as important ethical fields of combat. The discussion throughout is conducted in a clear, well-organized manner and should be enlightening for those seeking beginning guidance in these matters.

I found particularly interesting the analysis of the concept of personhood, whose differing definitions and implications are shown to underlie the vexed debate over the morality of abortion and also to strongly influence arguments about euthanasia. This subject is broken down into its component parts—active and passive and voluntary, unvoluntary, and involuntary—in a way that encourages orderly thinking about these questions,

This is not a casebook, although a few clinical examples are presented. Dr. Kantor attempts to leaven his essentially deductive approach with practical considerations and, on occasion, offers advice on how to proceed in a particular situation. An example is the course of action to be taken with a patient hospitalized with an incurable terminal illness for whom do-not-resuscitate orders may become an issue. Dr. Kantor believes such a patient should be "given his diagnosis and informed that termination of treatment is an option open to him." This advice also illustrates how his preference for patient autonomy and self-determination affects his judgment. An opposing view might suggest that although many, possibly even most, patients might properly be dealt with this way, there should also be room for a clinical determination that certain patients will suffer so much from being informed of their imminent demise that the proper and more humane ethical posture might be the utilitarian decision not to so inform them. On similar grounds it is also possible to disagree with the statement that "the physician's role qua physician to treat illness is taking second place to his fundamental being as a person obligated to respect and recognize the dignity and self-determination of his patients."

For purposes of this review, the chapter on "Psychiatric Ethics" deserves somewhat fuller discussion. Dr. Kantor holds that mental health and mental illness depend on the concept of normality and deviance from normality. As he rightly points out, the different meanings attached to normality influence the way in which deviance or mental illness is regarded. If normality is seen in statistical terms, deviance in the sense of holding unpopular views can be labeled illness, as has in fact happened in the Soviet Union and as Thomas Szasz claims is also true in the United States. Dr. Kantor questions whether mental illness is totally culture-bound, and he seems to adhere more to essentialist than statistical concepts of normalcy. These allow certain kinds of behavior deviating from an essential human quality to be considered evidence of mental illness. But what this quality is that has been transgressed is seen differently by the four theories. The author himself opts for autonomy and believes that current thinking accepts substantial departure from autonomy as indicative of the presence of mental illness. But how are we to determine when an individual lacks autonomy to a degree that makes him or her irrational? All answers to this question have profound ethical implications. These come into play preeminently when the time comes to consider depriving individuals of their liberty in order to treat them for purported mental illness. Dangerousness to self and others has become the major justification for such action in the United States, and although the author sees ethical conflicts inherent in both kinds of dangerousness, in accordance with his leaning toward the preservation of autonomy as the main determinant of ethical behavior, he does not question the morality of relying on this standard. Again, and here I should confess my own bias toward a chastened paternalism under the utilitarian banner, it can be argued that the bracing but harsh winds of autonomy need to be tempered for some mentally ill people by the addition of *parens patriae* criteria for involuntary hospitalization.

In his discussion of the right of the mentally ill to refuse treatment, Dr. Kantor is mistaken when he says that this is now a recognized right in this country. In fact, it is recognized by less than half the states and not in federal law.

Medical Ethics for Physicians-in-Training has the virtues and defects of any attempt at a single-handed treatment of a broad subject. It avoids the diffuseness of edited volumes, necessarily and consciously at the cost of completeness. The particular point of view espoused by the author may spawn disagreement by some, but it also focuses attention on many difficult ethical issues. On the whole, this is a useful book that will benefit medical students and many physicians.

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Handbook of Psychiatry and the Law, *by Ebrahim J. Kermani, M.D. Chicago, Year Book Medical Publishers, 1989, 292 pp., $34.50 (paper).*

Reading and comprehending books written on psychiatry and the law can be a challenging task for many psychiatrists, including those who are forensically inclined. Although many of these books focus mainly on such traditional topics as the right to treatment, the right to refuse treatment, civil commitment, the suicidal patient, the violent patient, malpractice, and confidentiality, Dr. Kermani's *Handbook of Psychiatry and the Law* endeavors not only to cover these topics but to provide breadth of the subject matter at the interface of psychiatry and the law. Less often discussed topics such as the legal aspects of alcoholism and drug addiction, psychiatry in death penalty cases, First Amendment rights of children, the rights of handicapped children (including those afflicted with AIDS), and surrogate parenting are given substantially equal billing with the traditional topics.

Dr. Kermani organizes his topics around actual court cases. Such cases are instructive because they are generally the so-called landmark cases that have greatly affected legal thinking and consequently the regulation of psychiatric practice. For instance, although most readers are probably familiar with such cases as *Tarasoff v. Regents of the University of*

California, Dr. Kermani includes several other cases having far more influence on medical and psychiatric practice, such as *Canterbury v. Spence,* which involves informed consent. Also included are recent legal cases such as the controversial *Baby M* decision, which has affected the future of surrogate parenting.

Many of the illustrative legal cases belong in the recommended list of landmark cases that should be known by those who take the forensic psychiatry subspecialty Board examinations administered by the American Board of Forensic Psychiatry, Inc. Although the cases may not be described in sufficient detail in the book to help the candidate successfully pass the forensic psychiatry examinations, they contain enough of the highlights to provide a quick overview of each and to introduce other psychiatrists and mental health professionals to the world of the forensic psychiatrist. What may be equally important for the reader to grasp is the sometimes astonishing reasoning that has led to these major legal decisions. In any event, for both adult and child psychiatrists, *Handbook of Psychiatry and the Law* provides a thorough grounding in the many aspects of psychiatry and the law and can also easily serve as a good encyclopedia-type reference to keep on the bookshelf.

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The Solace Paradigm: An Eclectic Search for Psychological Immunity, *edited by Paul C. Horton, Herbert Gewirtz, and Karole J. Kreutter. Madison, Conn., International Universities Press, 1989, 464 pp., $65.00.*

The premise of this book is that there is "much room for expanded examination of the growth and development of religious feeling from the simplest, most primitive form to its most elevated, transcendent states. The Freudian approach to religious experience has been too cold, too idea bound, too prejudiced." This book presents a new testament in psychiatry, derived from the writings of Bion, Bowlby, and Winnicott. It is religious in that it embraces the reparative function of solace as "an overarching concept"; the transitional object is its vehicle and central to dealing with separation and loss. Solace is presented as the most appropriate term to describe the psychotherapist's means for compensating for the patient's separation from parents and healing the natural schism between fantasy and reality. Such is the lifelong exercise and the basic psychological issue behind the metaphor of loss of Eden.

Although some contemporary analysts perceive the analytic environment as "holding" in itself without a conscious effort by the analyst, there is a longstanding tradition of mistrust of nurturing in traditional psychoanalytic writing. Extension of solace by the analyst is seen by a large number of analysts as allowing the "enemy" of reason and truth to enter the room.

Some readers will find the fervor of conviction at the beginning of this book inspiring; others given to cooler perspectives and treatment may resist such enthusiasm. The wish to convince the not-yet-converted also leads to interesting but purely speculative attempts at establishing neurobiological and evolutionary underpinnings for the solace paradigm. Understandably, since the editors are attempting to stake a claim in already occupied territory, a full attempt at establishing legality will take another volume. The reader who is not initially convinced should read on; I found many helpful directions for psychotherapeutic management.

The whole of the first section on theory is extremely helpful in reestablishing understanding of the concepts. The presentation of the ideas of Winnicott and Rappaport includes an extremely sympathetic and illustrative vignette by Cappolillo of the enchantment in childhood from both the child's point of view and that of the analyst. This is an engaging and revelatory perspective on the nature of creativity. Grotstein presents many of the complex affective issues of interpersonal theory involving transitional objects. The chapter by Modell is his usual scholarly and textured exploration of the depth of the importance of the concept of the transitional object. Silver, Glassman, and Cardish write on the capacity to be soothed.

The second section presents seven new formal research studies. This is a somewhat surprising feature of this book; research has usually been *within* the therapeutic frame, but this section presents research *on* object relatedness with formal protocols as well as naturalistic studies and observations.

The third section presents "special research": cross-cultural observations of transitional phenomena in widely diverse cultures and geographies and a chapter on the role of early writing as transitional object.

The fourth section, on clinical research and applications, has some wide-ranging views on the uses of transitional objects and solace. There is a chapter by Coleman on object relatedness and the problems of treatment of the difficult adult inpatient. Giovacchini addresses the developmental factors in object relatedness. "Defective soothing" occurs with ineffective parental soothing patterns. Soothing is a primary organizer of personality in this view. There are other chapters of interest in this section as well.

This book has paradigmatic aspirations. This is a passionate call for shifting psychotherapy and psychoanalysis away from the intrapsychic views of inhibition and toward interpersonal issues of separation. Those of us who have become interested in the brain and in burgeoning neuroscience, who have been dealing primarily with the anxiety of separateness by use of benzodiazepines and antidepressants, may have some difficulty in seeing the importance of a relatively small theoretical shift within a developmental framework from classical psychoanalysis toward object relations theory and the solace paradigm. Yet a return to the elegant and textured ideas of Bion, Winnicott, and Modell, among others, is refreshing and absolutely relevant to contemporary therapy of all kinds and combinations.

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FAMILY VIOLENCE AND CHILD ABUSE

Family Violence: Emerging Issues of a National Crisis, *edited by Leah J. Dickstein, M.D., and Carol C. Nadelson, M.D. Washington, D.C., American Psychiatric Press, 1989, 266 pp., $21.95.*

The daily stories of family violence in our newspapers and on our television screens may cause familiarity and habituation, so that we do not really see or hear them. Thus we proceed undisturbed to ignore this increasingly serious problem. The monograph *Family Violence* is an outgrowth of a presidential symposium at the 1986 annual meeting of APA.

Dr. Carol Nadelson, the first woman president of APA, chose the topic in an attempt to publicize and bring attention to family violence. One statistic appears in many chapters: "*Family violence of some kind currently occurs in half the homes in the United States at least once a year*" (p. xii). The authors of the chapters citing this statistic—Elissa P. Benedek, Elaine Carmen, Judith Herman, Deborah Williams-White, and Marion Zucker Goldstein—describe in some detail the different groups who are seriously and frequently abused: children, the elderly, and women. The vignettes in these chapters are alarming. Other authors describe treatment programs that are directed not only to the abused but to their abusers, their social systems, the workplace, the criminal justice system, and the mass media. These treatment programs are described mostly in early stages, and many of the authors emphasize the pressing need for implementation and further research.

In their concluding chapter, the editors emphasize the importance of the helping professions joining with self-help groups, government agencies, and educational institutions to "assume responsibility for helping to change social institutions and child-rearing practices implicated in predisposing people of all ages to family violence" (p. 238). Their broad emphasis is a call to the helping professions not only to read the newspapers and the professional journals with statistics on this issue but to take action.

It would have been helpful in the concluding chapter to have a summary table of the main facts and figures (i.e., the overall statistics on abuse of children, the elderly, and others). In addition, a table with a summary of the important characteristics of preventive programs, which are embedded in several chapters, would have been useful for people planning such programs. The topical bibliography is an aid for both informed and uninformed readers because it is quite diverse. The appendix of contact agencies is informative but somewhat limited in scope.

This book is recommended reading for all mental health professionals to inform and augment our limited awareness of an important sociopsychological problem that is increasing at an alarming rate and has devastating effects.

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Beyond Sexual Abuse: Therapy With Women Who Were Childhood Victims, *by Derek Jehu with Marjorie Gazan and Carole Klassen. New York, John Wiley & Sons, 1988, 352 pp., $64.95.*

For experienced general therapists as well as for residents and medical students who, for a variety of reasons, have avoided asking all patients, regardless of gender and age, about a childhood history of sexual abuse, *Beyond Sexual Abuse* is an extraordinarily complete, in-depth, sensitive, informative, and well-written manual and clinical report. Derek Jehu, Professor Emeritus of Psychology at the University of Manitoba and Director of the University's Sexual Dysfunction Clinic, and therapists Marjorie Gazan and Carole Klassen describe the theory behind their clinical research and the treatment protocols they developed in working with 51 adult women who experienced childhood sexual abuse. The authors offer clear, usefully detailed explanations and references for any question that might arise in treatment. For example, victims' reactions of guilt may persist into adult mood disturbances, and fear into later phobias. Although reactions such as avoidance, denial, and dissociation can serve as coping strategies at the time of the abuse—often the only ones available to a child—they may persist as inappropriate ways of handling other life stresses. The authors explain why they did not include men victims, yet go beyond this statement to offer theory and treatment suggestions. They also do not neglect specific treatment issues for lesbians.

The chapter subheadings are listed in the table of contents with their page numbers for extreme ease of reference. The first section of the book includes four chapters about the prevalence and nature of child sexual abuse. Even in these more commonly known areas, facts and case examples are included that offer useful clinical information and techniques in an unusually readable form. The chapter on "Families of Sexually Abused Children" details in clear chart form the problems characteristic of both parents and child victims, such as a "milieu of abandonment" and role confusion (e.g., "parentification" of the child).

In the chapter "Therapy With Women Who Were Sexually Abused," the authors state clearly that the protocols they developed and use are based on the cognitive behavioral model. They share their procedures of assessment, evaluation, and treatment of self-blaming and self-denigratory beliefs and processes as well as the outcomes in four excellent case studies of women and their partners. The authors even describe group sessions conducted for the patients' male partners.

Other chapters detail the women's interpersonal problems and relations with men and with their partners, their offspring, their families of origin, and their abusers. Sexual dysfunctions are also addressed—causes, assessment, evaluation, and treatment procedures. The one drawback, evident from the book's introduction, is that no mention is made of psychiatric evaluation before patients embark on this cognitive behavioral program. In addition, the authors state that only some women need physical examinations. They say that a medical examination is not necessary for all victims but is indicated in the following circumstances: "recent history of ill health, or physical symptoms apart from the sexual dysfunction, complaint of pain or vaginal spasm during sexual activity, recent onset of impaired sexual motivation with no apparent cause, e.g., when the victim believes the dysfunction to be due to a physical cause" (p. 246). Obviously, all female and male victims of childhood sexual abuse should be evaluated by a psychiatrist and have a complete medical workup before entering into a therapeutic program. The program described in *Beyond Sexual Abuse* is excellent; for example, the women are advised to keep journals, and they write letters to parents and other family abusers about their abuse experience and feelings.

Professor Jehu and his colleagues offer therapists an excellent volume that should be read by all medical students as well as health professionals in other specialties who, with knowledge gleaned from this valuable project, can recognize and refer untreated victims. All techniques included are described and illustrated in detail, from visual imagery to cognitive restructuring and muscle-relaxing techniques. Reading this book will be well worth the time and effort. It is not to be skimmed; in fact, it can be reread and referred to repeatedly.

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Soul Murder: The Effects of Childhood Abuse and Deprivation, *by Leonard Shengold, M.D. New Haven, Conn., Yale University Press, 1989, 335 pp., $35.00.*

"Soul murder" is a term with a past. Daniel Paul Schreber, the paranoiac judge whose memoirs Freud analyzed, used it to mean the loss of identity he had suffered, presumably from childhood sexual abuse. Dr. Shengold has appropriated the term to designate instances of repetitive sexual or abusive overstimulation alternating with neglect "deliberately brought about by another individual" (p. 17). These lead to loss of identity, including sexual identity. "What happens . . . is so terrible, so overwhelming, and usually so recurrent that the child must not feel it and cannot register it" (p. 25). The child has nowhere to turn but to the tormenting parent, whom the child must perceive, delusionally, as good. Psychiatrists familiar with such victims will feel the horror return when they read this clinical material.

This book discusses varied aspects of the problem, including brainwashing and recurrent themes involving rats experienced by the victims of soul murder. The author reviews the literary output of Dickens, Orwell, Chekhov, and Kipling, all of whom experienced soul murder as children. Shengold examines the effects of soul murder in these authors as they relate it in their writing. The problem with this device is that nearly every fictional example involves physical abuse or neglect, whereas nearly all of the actual patients presented experienced sexual abuse. Many readers may feel that the horror of reality is somehow trivialized when juxtaposed against the fictional examples.

Then there is the term itself. Murder is intentional, yet Shengold presents no evidence that child molesters intend to harm the child rather than to gratify themselves. "Soul manslaughter" might be a more accurate, if less dramatic, term. Murder is also final, yet Shengold discusses partial soul murder, and therapy may relieve some of the effects of soul murder.

Most of this book is fascinating; much is wise. But some is downright silly, outrageous, or both. Shengold seems to agree with Robert Fliess that "urination is a regular method for releasing cannibalistic impulses" (p. 97). He "guesses" that fathers are as likely to have sexual contact with prepubescent sons as with daughters. He contends that mother-son incest is less common than father-daughter incest because of the primal importance of the mother for the child and the son's anxiety lest he impregnate his mother. What about the parent's drives? Shengold seems to be putting the onus squarely on the victim. In another sentiment that will enrage many readers, he blames a mother for her son's molestation because she had left him in the care of a baby sitter whose "homosexual proclivities were common knowledge in the family." Surely we have progressed far enough that psychiatrists no longer assume that gay men and women are dangerous.

This book will impress itself on the consciousness of readers, who should value its many intersecting ideas but be wary of buying into the author's prejudices.

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Reprints of Book Forum reviews are not available.

Letters to the Editor

Mania in an Elderly Man Treated With Bupropion

SIR: Several studies have reported that bupropion is effective in unipolar or bipolar depressed patients who are marginally responsive to or intolerant of conventional antidepressants (1). It has also been suggested that bupropion treatment is less often associated with manic states than are other antidepressant pharmacotherapies (2). We describe a 78-year-old man with a 30-year history of recurrent major depression that had been refractory to pharmacotherapy who became manic when he was treated with bupropion.

Mr. A sought outpatient treatment for a depressive syndrome of 14 months' duration. It was characterized by depressed mood; decreased energy, motivation, and activity; social withdrawal; hypersomnolence; anorexia; and feelings of worthlessness. He felt unable to think clearly. He was not delusional.

Mr. A had had eight major depressive episodes, the first at age 48. These had resolved spontaneously after 3 months. He had never required inpatient psychiatric treatment. He had no history of manic symptoms or of substance abuse. There was no family history of major depression.

He had been in generally good physical health but had had elective angioplasty and treatment with diltiazem hydrochloride in the preceding 6 months. A mental status examination showed depressed mood and mild psychomotor retardation, but cognition was intact.

Mr. A's symptoms failed to respond to the following trials of medication: desipramine for 6 weeks at a maximum dose of 200 mg/day, with a plasma level of 147 ng/ml; lithium carbonate for 4 weeks at 600 mg/day, with a plasma level of 0.63 meq/liter; and nortriptyline, in conjunction with lithium, for 8 weeks at a maximum dose of 75 mg/day, with a plasma level of 72 ng/ml. Mr. A also received fluoxetine alone, 20 mg/day, for 10 days, but this was discontinued because of nausea and anxiety.

After 6 days of treatment with 75 mg of bupropion each morning, Mr. A noted an increase in energy, motivation, and mood. Bupropion and diltiazem were discontinued on day 13 of treatment because he had developed irritability, grandiosity, extreme talkativeness, aggressiveness, decreased sleep, and decreased need for sleep.

Mr. A was distressed by his symptoms, which persisted. He was reluctant to take lithium. After 3 months, lorazepam, 0.50 mg p.o. at bedtime as needed, was started, and this decreased his symptoms, although his mood remained at a hypomanic level for at least another 4 months.

A switch from depression to mania occurs in 7%–17% of patients during pharmacologic treatment and occurs more frequently in bipolar patients. A drug effect is suggested when the switch occurs shortly after the initiation of antidepressant treatment.

It has been suggested that there is a relationship between age and vulnerability to mania during antidepressant treatment. During clomipramine treatment of recurrent unipolar depression, a switch to mania was noted in older patients (3). Jain and Young (4) noted that elderly manic patients with late onset (age >58 years) of their first manic episode more often had had antidepressant pharmacotherapy during their index episode.

The pharmacologic specificity of Mr. A's manic response is of interest. Bupropion's pharmacologic profile differs from that of other antidepressants. It does not include appreciable effects on the uptake of norepinephrine or serotonin or on monoamine oxidase activity, and it may include inhibition of dopamine reuptake (5).

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BETSY J. BITTMAN, M.D.
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Malignant Hyperthermia During ECT

SIR: Malignant hyperthermia, a life-threatening pharmacogenetic disorder of anesthesia, usually occurs in a surgical setting when susceptible patients are unwittingly exposed to potent inhalation anesthetics. However, since succinylcholine may trigger this syndrome, malignant hyperthermia may also occur during ECT, although a search of the literature between 1966 and 1982 (1) revealed no cases of malignant hyperthermia due to the use of succinylcholine during ECT. To our knowledge this is the first such report.

Mr. A was a 30-year-old man with a 7-year history of schizoaffective disorder. At the time of admission, he was catatonic, with severe psychomotor retardation, mutism, and withdrawal. He had responded poorly to treatment with various antidepressants, loxapine, and carbamazepine, although no untoward effects had occurred. He had had surgery with general anesthesia twice previously. There was no family history of problems with anesthesia. The findings of physical and laboratory evaluations, including CBC, thyroid function tests, chest X-ray, ECG, EEG, and a CT brain scan, were normal.

Informed consent for ECT was obtained from Mr. A and his mother, and loxapine and carbamazepine were discontinued 12 days before the first ECT. Mr. A received six bilateral ECTs with a MECTA SR-1 machine during 1 week. Anesthesia consisted of curare, 3 mg; atropine, 0.4 mg; succinylcholine, 60–100 mg; and methohexital, 40–90 mg. Treatment with loxapine, 10 mg b.i.d., was resumed before the last two ECTs.

Mr. A improved, but he became febrile (maximum temperature=101.8 °F) and rigid shortly after the last three ECTs. The temperature elevation persisted for several hours and remitted spontaneously. In addition, he developed tachycardia (180–190 bpm) and complained of muscle soreness and weakness. Creatine phosphokinase levels were not ascertained, although the urine color never became brown or dark, i.e., suggestive of myoglobinuria. ECT was discontinued and Mr. A was eventually placed on a regimen of bupropion, trifluoperazine, and benztropine. He was discharged 10 days after the final ECT, without fever or stiffness.

Two months later, Mr. A underwent a diagnostic procedure to evaluate his susceptibility to malignant hyperthermia. Muscle tissue for biopsy was taken from the thigh; sedation and femoral nerve block and lateral femoral cutaneous nerve block with the local anesthetic mepivacaine were used during this procedure. The muscle was tested according to a standardized protocol (2) for its response to halothane and caffeine. The response to caffeine was normal. The maximal contracture response to 3% halothane was 0.9 g (the normal threshold is 0.7 g). In addition, there was a contracture response of 0.5 g to 1% halothane, which is also above the normal threshold. Results of muscle histology testing were normal.

Mr. A manifested symptoms typical of the malignant hyperthermia syndrome: elevated temperature not due to infection, muscle rigidity, and tachycardia. The muscle contracture response to halothane was abnormal, indicating susceptibility to malignant hyperthermia. The fact that Mr. A had previously received anesthetics did not rule out susceptibility to malignant hyperthermia, since approximately 50% of susceptible individuals have had previous anesthesia without incident (3).

Grigg (4), in a similar case, noted the similarity between neuroleptic malignant syndrome and malignant hyperthermia. He speculated that treatment with neuroleptics may "sensitize" individuals to hyperthermic reactions when they are exposed to anesthetics, even anesthetics not normally associated with malignant hyperthermia. In swine, however, neuroleptics may actually delay the onset of malignant hyperthermia or attenuate its severity when they are administered prior to halothane (5). The role of loxapine in this case was unclear. Conceivably, malignant hyperthermia may represent a pharmacological derivative of a broader spectrum of hyperthermic disorders that can be provoked and modified by a variety of agents.

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ARTHUR LAZARUS, M.D.
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Fluoxetine as a Cause of SIADH

Sir: We present a case of the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) caused by fluoxetine. The patient's osmolality and serum sodium levels returned to normal after discontinuation of the drug. Fluoxetine is an antidepressant drug unrelated to the tricyclic or tetracyclic antidepressants.

Ms. A, a 53-year-old woman with a history of depression, had been taking fluoxetine, 20 mg/day, for 2 weeks before her admission to the hospital. Upon arrival at the emergency room, she complained of fatigue of 2 days' duration. Her chief complaint was lightheadedness, occurring over a period of 24 hours, which she described as a "swimming head." Her depression had been treated with trazodone hydrochloride and fluoxetine 9 months previously. At that time she had had an onset of similar symptoms about 1 week after starting these medications (she was not taking any other medication). Consequently, she discontinued the trazodone and fluoxetine without informing her physician. Two months prior to this presentation, her serum chemistry had been normal, with a serum sodium level of 137 mmol/liter.

In the emergency room Ms. A was alert and oriented and in no acute distress. Her blood pressure was 130/80 mm Hg and her heart rate was 100 bpm without orthostatic changes. Results of a physical examination were unremarkable except for left strabismus. Her serum chemistry was normal except that her sodium level was 122 mmol/liter and her chloride level was 90 mmol/liter. Her serum osmolality was 258 mosm/liter (normal range=276–305), urine osmolality was 385 mosm/kg (normal range=500–800), urine sodium level was 102 meq/liter, and urine potassium level was 37.1 meq/liter. The patient's low serum osmolality, sodium, and chloride levels were consistent with SIADH. Her ECG, chest X-ray, thyrotropin and T_4 levels, and CT scan of the head were normal. Forty-eight hours after the fluoxetine was discontinued, Ms. A's serum sodium level was 141 mmol/liter and her chloride level was 106 mmol/liter. The serum sodium level remained normal, and after the patient had been asymptomatic for 3 days, she was discharged from the hospital.

Drugs such as chlorpropamide, antineoplastic drugs, tricyclic antidepressants, and diuretics produce SIADH. Hypothyroidism and psychosis can induce SIADH (1). Fluoxetine challenge would be the most appropriate way to demonstrate the cause-effect relationship between the drug and SIADH, but we were unable to obtain the patient's consent for this.

Our findings agree with those of Hwang and Magraw (2) in indicating that fluoxetine should be considered as a possible cause of SIADH. There appears to be a relationship between serotonin reuptake blockers, which include tricyclic antidepressants and monoamine oxidase inhibitors, and SIADH (3). Fluoxetine is a selective serotonin uptake blocker. Platelets of patients treated with fluoxetine have diminished uptake of H-serotonin. The degree of inhibition is proportional to the plasma concentration of fluoxetine (4). There is also speculation that fluoxetine blocks serotonin uptake by *p*-chloroamphetamine in the CNS. However, the syndrome resolved much faster in our patient after the drug was discontinued. Case reports by Hwang and Magraw (2) and Cohen et al. (5) do not include information about their patients' hepatic and renal function. Possible explanations for the prompt resolution of our patient's reaction may be related to her younger age and normal liver and renal function. The possibility that fluoxetine-induced SIADH may be mediated by nonserotonergic mechanisms such as the catecholamines cannot, however, be excluded.

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Suicidal Ideation Not Associated With Fluoxetine

SIR: The November 1990 issue of the *Journal* contained my case report (1) of a patient who developed suicidal ideation while taking fluoxetine, as in a series of six patients reported by Teicher et al. (2). I wish to report important follow-up information which suggests that the occurrence of suicidal ideation in this patient while he was taking fluoxetine was merely coincidental.

Since the case report was submitted, Mr. A has been hospitalized twice for depressive relapses with suicidal ideation while he was taking imipramine and disulfiram. He has been free of substance abuse and he has not taken fluoxetine for 7 months, well past the half-life of this medication. Intermittent extreme suicidal ideation of the same quality has occurred in this patient when he had levels of imipramine plus desipramine between 241 and 432 mg/dl.

A recent retrospective study of 1,017 depressed patients (3) showed no statistical significance for emergence of suicidal ideation during different somatic therapies. The medications studied included 1) fluoxetine alone, 2) fluoxetine and a tricyclic antidepressant, 3) a tricyclic with or without lithium, 4) monoamine oxidase inhibitors, and 5) other agents. Furthermore, up to two-thirds of depressed patients report suicidal ideation at some time during their illness (4). Given these facts, it is unlikely that fluoxetine has any relationship to the development of suicidal ideation.

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Correction of Drug Promotion Item

SIR: During the recent Collegium Internationale Neuropsychopharmacologicum (CINP) meeting in Japan, a promotional item was distributed with a copy of the Hamilton rating scale that included the name of our drug Tolvon. It was by no means our intention to indicate that the late Professor Hamilton had endorsed this drug or that he had been associated with it. We are sorry to learn that close colleagues and the immediate family of Professor Hamilton have been disturbed by this publication, particularly in view of the fact that, in helping with drug trials, Professor Hamilton was always impartial and insisted that his name should not be used to sway a decision one way or another.

If we have inadvertently given any other impression, we should like to state that this was certainly not our intention.

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Cross-Cultural Issues and *Treatments of Psychiatric Disorders*

SIR: We write this letter to express our profound disappointment that there are but three cross-cultural index entries in the recently released three-volume treatise by the APA Task Force on Treatments of Psychiatric Disorders (1). Indeed, while there is total omission of Native-American issues, the only chapter that includes references to "blacks," "Orientals," and "Hispanics" (sic) is on sexual dysfunctions (chapter 216, pp. 2380–2383). We fear that this unfortunate sociocultural scotoma does little to reassure the reader that psychiatrists do not share the myths and prejudices held by a generally ethnocentric society which often ignores the multiclass, multiracial, and multilingual reality of its citizens. This failure is specially disturbing when so many prominent American scholars have devoted a significant portion of their careers to the scientific study of effective therapies for the socioculturally and racially diverse.

In the 1970s psychiatric researchers and clinicians suggested that traditional psychotherapeutic techniques might alienate linguistic-minority patients. During the 1980s therapists were warned against ignoring intragroup differences and advised to attend to the legacy of rampant discrimination and stereotypes expressed in a literature that often spoke of the socioculturally different as pathological and culturally deprived. As we enter the 1990s, we must continue to examine the connections between the biopsychosociocultural distress of stigmatized and socially devalued ethnic minorities and the sociopolitical realities of their reference groups. In this manner, hopefully, we will not blame the victim, nor ascribe to culture or race what may be socioeconomically related, nor interpret as psychopathology what could simply be the effects of limited proficiency in the English language, nor ultimately continue to deny the ideological biases of many of our traditional treatment perspectives.

In short, we are deeply troubled by the publication of this treatise that appears to deny the current trend in our mental health field toward a pluralistic therapy model. We strongly believe that this work has done a disservice to our constituents, to patient care, and to psychiatric education and research.

Obviously, there are many ways for APA in general and the task force in particular to demonstrate their recognition of the value and importance of sociocultural influences in the manifestation and treatment of mental illness. Perhaps a point of departure is to solicit commentary and contributions to any relevant APA-sponsored publication from individual members who are active in the area of ethnocultural psychiatry, as well as from professional and scientific organizations whose raison d'être is the promotion of transcultural psychiatry and cultural knowledge.

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1. Treatments of Psychiatric Disorders: A Task Force Report of the American Psychiatric Association. Washington, DC, APA, 1989

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Dr. Karasu Replies

SIR: I am sorry that a number of important members of our profession have found *Treatments of Psychiatric Disorders* lacking in cultural sensitivity and assert that "the work has done a disservice to our constituents." I am especially troubled by the implication that the work may have unwittingly or, worse, intentionally devalued ethnic minorities. Let me put the intent aside and carefully scrutinize the process and final content.

Treatments of Psychiatric Disorders was the last in a series of publications of the task force. The previous one devoted a chapter to overall treatment planning, which included a discussion of race, ethnicity, religion, and social/cultural issues, as well as geographic and ethical factors (1). Regarded as a baseline for *all* treatment, these issues were not individually reintroduced and retailored to every diagnostic category, as perhaps they should have been.

We distributed the drafts of the projects to APA district branches and made them available to any organization that was interested. Here, the signers of this letter may have to share some of the burden of self-criticism. This is not a project that sneaked by; it was repeatedly discussed in its various levels of development at APA's many spring and fall meetings and was subject to open controversies and debates in meetings as well as in print (*Psychiatric News*, *New York Times*, etc.). How is it that these individuals who describe themselves as "active in the area of ethnocultural psychiatry" made no active move to see the material or to meet with the task force, as many other interest groups did? If one's "raison d'être" is the promotion of transcultural psychiatry, what is the reason for such noninvolvement? We would all agree, I believe, that "activity" is too narrowly defined if limited to ex post facto protest letter writing.

Nevertheless, as a task force, we should have targeted the distribution of the drafts to specific individuals and organizations with specific interest and expertise in ethnocultural psychiatry. For all these "we should haves" and other shortcomings of the project, I apologize on behalf of the task force and trust that its future editions will reflect a greater ethnocultural sensitivity.

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Postpsychotic Depression

SIR: Michael Foster Green, Ph.D., and associates (1) found in their prospective assessment of the symptomatic vicissitudes of 27 patients with recent-onset schizophrenia or schizoaffective disorder "no distinctive postpsychotic pattern of onset for depression." Aspects of this paper are problematic. In the literature, postpsychotic depression is a traditional concept that is rather consistently described. The negative report by Dr. Green and associates may be due to their misidentifying the definition of the construct.

The definition of depression was restricted to the item cluster of depressive mood, guilt feelings, and suicidality from the authors' published modification of the Brief Psychiatric Rating Scale (BPRS). The clinical literature on postpsychotic depression, however, gives emphasis to phenomena such as massive inertia and passivity, frequent neurasthenic complaints, strong elements of isolation, and reports of emptiness or lack of feelings (2). In more chronic patients these elements of "pseudodepression" are often predominant. To omit such manifestations is a critical error if one purports to investigate the traditional concept. Vegetative, "pseudodepressive" elements are also a part of the Hamilton Rating Scale for Depression. This instrument was used by Mandel et al. (3) to investigate prospectively the appearance of postpsychotic depression in recently discharged, nondepressed schizophrenic patients. The observed incidence of 25% is consistent with other reports (4). Siris et al. (5) also used the Hamilton scale to define patients with postpsychotic depression, who then benefited from a trial of imipramine. This supports the discrimination of postpsychotic depression, which often develops in patients taking neuroleptics, from depression in acutely ill patients for whom tricyclic treatment is of no appreciable benefit over neuroleptic treatment alone (6).

The criteria used by Dr. Green and colleagues to define an episode of depression make it likely that what were rated as new episodes were simply vicissitudes of continuous depression. Minimum criteria for a new episode consist of two BPRS depression ratings of 4 that could follow a remission consisting of two BPRS depression ratings of 3. It is entirely conceivable that many patients traversed the well-documented course of an exacerbation of depressive symptoms that was concurrent with but outlasted an exacerbation of psychotic symptoms, i.e., a "revealed" depression (4). The patient could fulfill one of the criteria for depression during psychotic exacerbation, dip to a score of 3 and have a "remission" of depression as a temporary fluctuation, then resume having depressive symptoms at a level of 4. This would count as a new exacerbation.

Schizophrenic patients are psychiatry's most symptomatic patients. With the onset of delusions and hallucinations, erosion of important areas of personality, and loss of instrumental functioning, they become depressed for many reasons and with a variety of symptomatic patterns. It is important to study these various depressions—their causes, courses, and treatments. However, defining criteria need to capture the concept of interest.

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SIR: Dr. Green and associates may have misidentified the timing of postpsychotic depression. Also, the data reduction and analysis in their study limit the interpretation of the findings.

The time period defining a postpsychotic depression is unclear. Most reports place it vaguely during remission of florid symptoms and especially (in the older literature) after discharge. Dr. Green and associates are to be commended for introducing specificity to this temporal sequence, but their definition of postpsychotic as the 8-week period after the end of a psychotic episode is rather narrow. Other observers might include as postpsychotic part or all of three of the six time periods mentioned by Dr. Green and colleagues. Their 8-week period sandwiched between "long after psychotic onset" and "other" does not reflect general views of the traditional concept. For example, in a life-table analysis of onset of postpsychotic depression, Mandel et al. (1) found that most of their cases were not detected until 10–45 weeks after discharge.

The approach of Dr. Green and associates to statistical analysis makes interpretation difficult. The chi-square statistic presumes independence of the data. Only nine of the 27 patients suffered just one episode of depression. The remaining 54 episodes were experienced by 18 patients. This made an average of three episodes per patient for two-thirds of the patient group. Fifteen of these 18 had onsets of depression in more than one time period, and it is unlikely that these were truly independent episodes of depression. Interdependence in the type of data set reported by the authors could be eliminated by using only the first depressive episode for each patient. This would require a much larger number of patients. The data could then be legitimately analyzed by chi-square. In this way one could also ask questions regarding factors that might discriminate between patients whose data are in different cells.

At the heart of Dr. Green and associates' conclusion that postpsychotic depression was not observed in this cohort is the failure of the observed frequency of depression to exceed the expected frequency. A final problem rests in the absence of normative base rate data to define expected frequency. Why should any of these patients be expected to be depressed at any time? We think there are several reasons, and these reasons differ by time period. Dysphoric affect, including depression, is a defining component of a prodromal phase or early relapse (2). Depression occurs in more than one-half of patients as a symptom manifestation of a psychotic episode, especially in early cases (3). Depression is common after florid psychosis, sometimes as a continuing phenomenon and sometimes (hypothetically) as postpsychotic depression. Demoralization, certain negative symptoms, aphanisis, and so forth are often observed later in the course of illness and may overlap with depression. If such considerations are germane, the validity of any of these propositions cannot be tested by comparing the frequency of BPRS depressive symptoms by time periods. We believe that depression in cohorts of early schizophrenic patients is expected to be higher than normal population base rates for several reasons, and these reasons predict that depression will be observed in all time periods.

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Dr. Green and Associates Reply

SIR: Drs. McGlashan and Waltrip express concern about our definition of depression, which was admittedly restrictive. Instead of diagnosing major depressive episodes, we assessed depressed mood and suicidal thoughts with the expanded version of the BPRS (1). This means of assessment can raise reasonable concern that we were missing certain elements associated with postpsychotic depression. However, an article by McGlashan and Carpenter (2) indicated that the most discriminating symptoms of postpsychotic depression were "feeling unhappy" and "life not worth living." We used items with similar content from the expanded BPRS. Some of the "pseudodepressive" aspects of postpsychotic depression would be missing from our depression index, but many would be included in the withdrawal/retardation factor of the BPRS. Interestingly, this factor shows the same pattern of onset as the depressive symptoms: exacerbations of withdrawal/retardation begin disproportionately more often in the concurrent time period and not in any other period. Such a finding argues against the possibility that we would have found a pattern of postpsychotic onset if we had included these pseudodepressive elements in our definition. We realize that the vegetative signs of depression are missed by the BPRS scales, and we agree that the Hamilton Rating Scale for Depression would have provided a richer picture of the quality of depression.

Ms. Summerfelt and Dr. Carpenter point out that our use of the chi-square test might not have been appropriate because some of our subjects contributed multiple depressive episodes to the data, and thus the observations were not independent. Our principal finding, an unexpectedly large number of depressive episodes with onset concurrent with psychotic exacerbation, did not appear to be an artifact of multiple entry of the same subjects. For one thing, expected frequencies were calculated separately within each case, which takes into account individual differences in base rates for both depressive episodes and time at risk in each period. The concurrent time period constituted only about 3% of the observed time for the average subject, but 14 of the 63 depressive episodes (22%), representing 13 different subjects (48% of the subjects), occurred during this period. Nevertheless, we agree that perhaps our statistic is better termed a "chi-square-like" statistic. We were not entirely sure how many degrees of freedom to use in evaluating the significance of the statistic across the six cells of our design. Six cells would normally yield five degrees of freedom for the chi-square, and that is what we elected to use. In view of the extremely high value we obtained, it was our judgment that the issue was, in practice, inconsequential.

We have now reevaluated the results by performing an approximate randomization test (3), and it appears to confirm our judgment. The procedure is as follows. Each depressive episode is randomly assigned to one of the six time periods, with the probability of assignment proportional to the total number of weeks for that time period. These assignments are completely random but suffer from the same lack of independence as the statistic we reported in the article. We repeated this procedure 1,000 times and examined the empirical distribution of our statistic. This is a highly robust test. The highest value for the 1,000 tests was 15.74; the value we obtained in the real data was 72.83. Since no value this high occurred in 1,000 trials, we conclude that the p value is less than 0.001. We also examined the separate test for the concurrent time period. The highest value in the randomization was 11.38, compared with 67.20 in our real data (again, empirical $p<0.001$).

A separate issue is whether we failed to distinguish between clinically meaningful episodes and minor fluctuations in symptoms. Our inclusion of "mild" depressive episodes may have been too liberal, and we have now reanalyzed the data after eliminating the mild depressive episodes, so that any new depressive episode would require a minimum score of 5 on at least one of the depressive items. Using the approximate randomization test we have described, we found essentially the same results. None of the time periods differed significantly from chance except for the concurrent period ($p<0.001$). Twenty percent of the depressive episodes occurred in the concurrent period, which occupied 3% of the total follow-up period. The results were not overly influenced by a few individuals; the nine depressive episodes in the concurrent period were contributed by nine different subjects.

It might be helpful to clarify the distinction between the *onset* of depressive episodes during the postpsychotic period and the *persistence* of depressive symptoms into the postpsychotic period. Our study considered only the timing of the onset of depressive episodes, not the severity of depression in each of the time periods. Hence, we did not assess the presence of depressive mood in the postpsychotic period. Our data suggest that depressed mood did not begin in the postpsychotic period, but it might have continued into this period. Our conclusions are entirely consistent with those of McGlashan and Carpenter (2, p. 17): "Our findings indicate that patients generally do not develop a depression de novo in the postpsychotic period but that the depression represents an already existing symptom complex that remits more slowly than the acute psychosis." Perhaps ambiguity could be reduced if a depression that remains after the remission of psychotic symptoms was referred to by another term, such as "lingering depression," to distinguish it from a depression that begins in the postpsychotic period.

The suggestion to compare the number of depressive episodes to that of a normal sample is reasonable, and would address the absolute frequency of depression, but not the temporal sequencing of symptoms. Ms. Summerfelt and Dr.

Carpenter argue that schizophrenic patients may be more depressed than normal control subjects in every time period. If so, how would this finding be interpreted? Would it be helpful to postulate a different etiology and nosology for depression in each time period, or would it be more parsimonious to conclude that schizophrenic patients have more depression in general than do normal control subjects (because of factors such as stressful life events, reduced processing capacity, or abnormal neurotransmitter systems)?

Finally, the finding by Mandel et al. that Ms. Summerfelt and Dr. Carpenter cite is potentially problematic. If patients can suffer "postpsychotic" depression any time up to 45 weeks after a psychotic episode, the question becomes, What does *not* constitute postpsychotic depression? To be sure, some depressive episodes occurred in each of the time periods in our study. We think that the term "postpsychotic depression" implies a clinical (if not a causal) connection between psychotic and depressive episodes, and we specifically evaluated whether this connection takes the form of an increased frequency of onsets of depression following onsets of psychotic symptoms. Our breakdown of the various time periods was admittedly arbitrary, but we failed to find any deviation from random occurrence of onset of depression except for the concurrent period.

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Hyperprolactinemia and Major Depression

SIR: The letter to the Editor "Treatment of Hyperprolactinemia in Major Depression" (1) by Suzanne Holroyd, M.D., and Mitchell J. Cohen, M.D., has caused a minor depression in this endocrinologist who scans her husband's psychiatric journals. If psychiatrists were to heed the last sentence, "Correcting elevated serum prolactin may be necessary for successful treatment of depression," an unwarranted use of dopamine agonists in depressed patients could ensue.

It is my view that the authors' conclusion cannot be substantiated. The patient was treated with eight ECTs followed by imipramine, both of which have been established as effective treatments for depression. In my practice, hundreds of patients with elevated prolactin levels—the highest over 8,000 μg/liter—have not shown an unusual incidence of depression. Psychiatrists use many drugs that elevate prolactin levels significantly (e.g., haloperidol), and no evidence of increased depression has been reported in these patients to my knowledge. Perusal of the references in the letter has not led me to conclude that elevated prolactin levels are associated with depression.

Drs. Holroyd and Mitchell suggested that the increased thyrotropin level could have been due to the local effect of the prolactinoma. On the contrary, a pressure effect from a pituitary tumor lowers the thyrotropin level. It is far more likely that previous lithium treatment was responsible, as they also suggested.

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Dr. Holroyd and Dr. Cohen Reply

SIR: We thank Dr. Vale and Dr. Raphael S. Good (1) for reading and responding to our letter. As Dr. Good points out, many medical disorders can present as psychiatric illness, and thus a thorough medical history and examination are needed as part of every psychiatric evaluation. We never meant to imply that such measures were "reserved" for refractory cases; rather, one reason for our case report was to point out another possible medical illness, prolactinoma, that could present as major depression and to remind psychiatrists to be alert to such possibilities.

Dr. Vale doubts the possible relationship between our patient's psychiatric illness and her prolactinoma, since the patient recovered when she was treated with ECT and imipramine. However, as we stated in our letter, this patient had already had adequate trials of ECT and tricyclics, as well as monoamine oxidase inhibitors, lithium, and neuroleptics, without effect. These previous trials were conducted at a large tertiary care center before the patient was referred to us. It was not until her prolactinoma was diagnosed and treated that she responded to ECT and pharmacotherapy. Also, this patient's major depression with psychotic features occurred without a family or personal history of psychiatric disorder and at the same time that other symptoms of the prolactinoma (i.e., amenorrhea, galactorrhea) appeared.

Dr. Vale also states that the patients in her practice who have elevated prolactin levels do not have a higher incidence of depression. First, it would be interesting to study these patients in a systematic way to confirm this impression. While many patients with a given medical disorder do not exhibit psychiatric symptoms, a relationship between the medical disorder and psychiatric symptoms in a certain subgroup of patients may well exist (for example, depression in patients with hypothyroidism). Why a subgroup of patients selectively exhibit psychiatric symptoms is a question only further research will answer.

Finally, the limited space for a letter to the Editor limited our references, too. We now add other relevant references (2–6) for further perusal of this interesting topic.

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Affective Spectrum Disorder?

SIR: James I. Hudson, M.D., and Harrison G. Pope, Jr., M.D. (1) have suggested the term "affective spectrum disorder" for eight disorders, namely, major depression, bulimia, panic disorder, obsessive-compulsive disorder, attention deficit disorder with hyperactivity, cataplexy, migraine, and irritable bowel syndrome. Since the criterion used for this nomenclature was the "specific antidepressant response" (the authors excluded from their evaluation disorders responsive to antimanic drugs and mood-stabilizing drugs), the correct term would have been "depressive spectrum disorder." The term "affective spectrum disorder" should include manic disorder, schizoaffective disorder, organic affective disorder, cyclothymia, dysthymia, etc. The authors excluded the first three disorders "since these conditions are already defined primarily by the presence of affective symptoms." But then so is major depression, which is, however, included in the spectrum concept. This seems quite arbitrary.

Also, the choice of the antidepressant response model is faulty. Antidepressant drugs, in addition to their obvious antidepressant effect, may have several other clinical effects. Therefore, the affective spectrum disorders showing response to treatment with antidepressants may really be responding to the nonantidepressant clinical effects of these drugs. If this is so, then these disorders should show a differential response to antidepressants. As pointed out by the authors themselves, obsessive-compulsive disorder responds differentially to antidepressants that act on serotonin. This observation defies the unitary concept of the proposed spectrum disorder. The authors justify this by saying that "the various forms of affective spectrum disorder . . . respond not to one but to three or more chemically different classes of antidepressants." However, chemically different forms of antipsychotics are used for the treatment of Sydenham's chorea, agitated depression, severe intractable hiccough, vomiting, Tourette's disorder, mania, schizophrenia, schizoaffective disorders, anorexia nervosa, and infantile autism. By the same analogy, these disorders should be called thought disorder (or cognitive) spectrum disorders. I do not think this approach is appropriate. All that can be said about these disorders is that they are antidepressant-responsive disorders and antipsychotic-responsive disorders, respectively. The argument can be extended to the use of benzodiazepines in treating anxiety disorder, status epilepticus, insomnia, myoclonic seizures, alcoholic withdrawal syndrome, and stage 4 non-REM sleep disorders and the use of carbamazepine in generalized tonic-clonic seizures, complex partial seizures, bipolar mood disorders, trigeminal neuralgia, digitalis-induced ventricular arrhythmias, impulse control disorder, and alcoholic withdrawal syndrome.

The term "affective spectrum disorder" connotes disorders of affect and its clinical spectrum. Drs. Hudson and Pope agree that the choice of the term is "arbitrary." Since these disorders resemble one another only in the one proven fact of response to antidepressants, I suggest that they should be, at best, called antidepressant-responsive disorders until future research provides data for (or against) the spectrum concept. Until then, the spectrum concept should be used, if at all, for the clinically similar affective syndromes or in the manner it was used by Winokur et al. (2).

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Dr. Hudson and Dr. Pope Reply

SIR: We agree with Dr. Ahuja that "antidepressant-responsive disorders" would be a more technically precise term for the family we have called "affective spectrum disorder." We would point out, however, that antidepressant response is only a marker for the proposed family, not its defining characteristic. In other words, there may be other disorders in the family that cannot be identified on the basis of antidepressant response but that nevertheless share the common etiologic feature which we have predicted in affective spectrum disorder. Disorders such as bipolar disorder and schizoaffective disorder may fall into this category.

Next, Dr. Ahuja argues that antidepressants may have several clinical effects beyond their antidepressant effects and that this might explain the differential response of different forms of affective spectrum disorder to various antidepressants. However, we noted in the introduction to our paper that it would be extraordinarily unlikely that *all* of the various classes of antidepressant drugs would have in common a second, entirely independent pharmacologic property in addition to the pharmacologic property by which they treat depression. Thus, it would be a remarkable coincidence if some forms of affective spectrum disorder were responding to the antidepressant effect of these drugs while other forms were responding to a separate effect that all of these different chemical families also happened to share.

Dr. Ahuja next argues that one could equally well posit a family of, say, antipsychotic-responsive disorders, but his example differs in two critical ways from the case of affective spectrum disorder. First, some of the disorders on his list, such as vomiting, are not disorders but individual symptoms of disorders. Second, and most important, antipsychotics only partially treat, or treat only individual symptoms of, most of the disorders on his list. By contrast, antidepressants, when fully effective, appear to treat the full clinical syndrome of each form of affective spectrum disorder rather than individual symptoms. The same argument would apply to Dr. Ahuja's other examples.

Nevertheless, even though Dr. Ahuja's examples differ in critical ways from the disorders in the affective spectrum disorder family, we would submit that they are not entirely trivial. For example, there may be significance in the fact that antipsychotic drugs work for both vomiting and psychotic symptoms; perhaps some common etiologic factor in these two types of symptoms will ultimately be found. Similarly, the fact that benzodiazepines are effective in anxiety, status epilepticus, and alcohol withdrawal suggests that these disorders may share a common etiologic "step." And the efficacy of anticonvulsants in both bipolar disorder and epilepsy, as we ourselves have noted (1), suggests that these disorders might share an etiologic "step" of considerable importance.

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JAMES I. HUDSON, M.D.
HARRISON G. POPE, JR., M.D.
Belmont, Mass.

Manual and Computer-Assisted Literature Searches

Sir: I was delighted to see an article in the *Journal* comparing manual and computer literature searches (1). However, I was dismayed at the misconceptions it contained. The manual search of the four journals the authors examined was quite extensive. They consulted four points (i.e., title, abstract, introduction, and method section) in searching through the journals. However, in the computer search, they used only three key phrases. In doing a computer search, one does not just type in key words and expect a complete bibliography. As any librarian will tell you, it is an interactive process. A medical librarian would have consulted the Medical Subject Headings list, which is used by the National Library of Medicine to index journal articles for their databases (e.g., Medline—part of the MEDLARS system). Some subject headings that I came up with include psychiatry; psychiatry department, hospital; consultants; and referral and consultation. A medical librarian experienced in on-line searching would combine these words, as well as using key words, to obtain a more comprehensive list of articles than the authors obtained.

Please do not take us back to the dark ages of flipping through journal issues in order to find relevant articles. Computer searching is an essential service today for the medical and psychiatric profession, but it must be done by a professional librarian to obtain all the relevant articles in a cost- and time-efficient manner.

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KAREN GAGNON
Kingston, Ont., Canada

Dr. Lyons and Associates Reply

Sir: In response to Ms. Gagnon's concerns about our study of computer-assisted and manual literature searches, several clarifications might be useful. We did not wish to imply that computer-assisted literature searches should not be undertaken; we merely demonstrated that they may not be thorough. The question then becomes, Did we give MEDLARS a fair test? Although our results are consistent with the reports of others (1–4), Ms. Gagnon asserts that if we had consulted a medical librarian we would have had greater success with this strategy. However, we did consult a medical librarian, and with her help we identified the three key word phrases that appeared to identify the most relevant studies and used these in our search. More to the point, however, many literature search systems have been designed for use without a librarian. Many are available on microcomputers; others can be accessed from home. Also, skilled research librarians are not available to all investigators. Given these circumstances, we believe that an empirical warning that even a fairly careful review might miss important articles is timely.

We would be curious to see whether, with the additional words that Ms. Gagnon suggested, she would be able to devise a more accurate search. Exhaustiveness is not the only criterion. A large number of false positives (articles identified by the search but not relevant to the review) can also present problems to an investigator. An obvious example is the use of the suggested heading "psychiatry," which would probably identify all relevant articles but also capture every other article in the field regardless of its relevance to consultation-liaison psychiatry. Even combinations of subheadings and key words can lead to an overidentification of articles.

We have no doubts that computer-assisted literature searches provide a great deal of assistance to investigators. We also know that medical librarians are invaluable. However, computer-assisted searches alone are probably insufficient for preparing a comprehensive review of a field of inquiry. We do not wish to take anyone "back to the dark ages"; however, we believe strongly that technology is not a replacement for thorough research.

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JOHN S. LYONS, PH.D.
DAVID B. LARSON, M.D., M.S.P.H.
JOSEPH BARETA, M.S.
JOSEPH J. ZORC, B.A.
Chicago, Ill.

Comments on the Review of *Cults*

Sir: I would like to comment on John Hochman's review of Marc Galanter's book *Cults: Faith, Healing, and Coercion* (1).

Dr. Hochman clearly has very strong negative feelings about the Unification Church, and he appears to be critical of Dr. Galanter for not joining him in an anti-Unification Church polemic. Although the reviewer touches on the importance of Dr. Galanter's research, he appears not to comprehend its unique value as an unbiased scientific study of a complex social phenomenon.

Dr. Hochman implies rather insidiously and without evidence that the results of Dr. Galanter's research were influenced by the relationship he developed with the Unification Church. As a member of the group participating in Dr. Galanter's first study of this organization (2), I was present at meetings with Unification Church officials in which the proposed research was discussed. No preconditions were set with respect to the questions that could be investigated or the results that could be published. Furthermore, a careful review of this study, of the book under consideration (3), and of Dr. Galanter's recent lead article in the *Journal* (4) gives ample evidence of the author's evenhandedness and lack of bias. Numerous points that could be used against the Unification Church are reported. Among these are the subterfuge used by certain branches of the church to obtain recruits; the fact that members dropped out of school and spent long hours proselytizing and selling to raise money for the organization; the fact that well after joining the church, members' scores on a well-being scale were lower than those of a comparison group in the general population; and the descriptions of the pressured engagement arrangements and mass weddings orchestrated by the Reverend Mr. Moon and church officials. Moreover, in his case reports Dr. Galanter shows the potential of cults both to relieve and to exacerbate psychiatric symptoms.

The clearly stated purpose of Dr. Galanter's pioneering work is not to attack or defend the Unification Church or any other organization but to investigate scientifically and attempt to explain how highly ideological, cohesive groups—including self-help movements such as Alcoholics Anonymous (AA)—exert their powerful influence over their members' beliefs and behavior. This is an issue of compelling psychiatric interest, but Dr. Hochman, involved as he is with his own agenda, barely deals with the valuable data and interesting interpretations offered by Dr. Galanter.

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ALEXANDER DEUTSCH, M.D.
New York, N.Y.

SIR: I object to John Hochman's review of the book *Cults: Faith, Healing, and Coercion* by Marc Galanter. The main thrust of that review was that Dr. Galanter, who was allowed to study the Unification Church, was not and cannot be unbiased because of the "relationships that develop between researchers and their subjects."

It is well-known that relationships can produce bias; two of the great thinkers of our times, Freud and Marx, contributed to the understanding of how this can occur. Unconscious bias is a hard charge for any of us to dispel completely; perhaps an accountant can disprove financial entanglements. Even a reviewer may be biased. Is it because Dr. Hochman approves of AA and the Marine Corps that he does not want them to be compared with the Unification Church? Are any of us really objective about Mormon missionaries, Jehovah's Witnesses, or Jews for Jesus?

What Dr. Hochman's review fails to convey to *Journal* readers is the great value of Dr. Galanter's conceptual framework and research findings for understanding the power of groups to change people. Dr. Galanter has courageously studied social phenomena that have long been virtually taboo for psychiatrists. Disconcerting to many, he has attributed a few positive features to a cult that is widely unpopular. Dr. Galanter's articles describing in detail the findings on which this book was based have been accepted by prestigious journals, including the *American Journal of Psychiatry*, for what these articles are—reasonable and objective attempts to understand charismatic groups from a scientific point of view.

WALTON T. ROTH, M.D.
Stanford, Calif.

SIR: Dr. Hochman's review of Dr. Galanter's book has come to my attention.

Dr. Galanter's latest contribution to the expanding literature on cults derives in part, I understand, from material already published in other places, including the *Journal*, and going back at least a decade. It is flattering that Dr. Hochman exaggerates my role as a source of what I, and other reviewers and concerned professionals of various kinds, regard as an important contribution to and synthesis of the literature on an important subject. I will confess to having served for some years as president of the New York Civil Liberties Union and to having represented some groups, including the Unification Church, as clients in my practice, which is to a large extent devoted to matters of civil liberties, including the free exercise of religion. Dr. Hochman is simply incorrect in his statement concerning the people and the relative size of the groups that constitute my clientele, but who my clients are and the sizes of their respective groups are no more significant in evaluating my concerns than the identities of Dr. Hochman's patients and what they pay him.

I regret the ad hominem tone of this response, but it cannot be otherwise when its etiology is a purported book review consisting of a direct personal assault on the author and snide, unfounded personal innuendoes concerning me.

JEREMIAH S. GUTMAN
New York, N.Y.

Dr. Hochman Replies

SIR: Dr. Deutsch asserts that *Cults* is unbiased because the author described some of the Unification Church's faults; Dr. Roth notes that the author simultaneously found redeeming features of the Unification Church. But to be unbiased, *Cults* would have to dispense equal treatment to similar groups; this does not occur.

Dr. Galanter blasts Synanon's leader:

> Synanon fell victim to the inflated role of Charles Dederich, its charismatic leader . . . . Dederich was arrogant and controlling, and in time even designated

> Synanon as a religion, granting himself a transcendent role far beyond that appropriate to the director of a drug treatment program. Unbridled power leads to feelings of grandiosity that may be difficult to withstand .... Power was concentrated in the hands of a single individual who proved ill fit to manage it. (p. 189)

Dr. Galanter fails to mention that Dederich oversaw a multimillion-dollar promotional sales business (called ADGAP) within Synanon. By contrast, he describes the Reverend Mr. Moon as a "successful minister and industrialist" (p. 130), accepting Moon's claim to head a "church" (even though he is simultaneously an industrialist) while rejecting Dederich's similar credentials.

Dr. Galanter derides the claims of the leader of the People's Temple, Jim Jones: "There were implicit demands for an intensification of commitment to Jones' idiosyncratic views, and increasingly bizarre beliefs came to be expected of these longstanding converts. Jones, for example, now claimed to be the reincarnation of Jesus, as well as Ikhnaton, Buddha, Lenin, and Father Devine" (p. 121). However, he offers nonjudgmental silence for Moon's claims: "He told his followers that as a youth, while he was praying on a mountainside one Easter morning, Jesus appeared in a vision and called on him to carry out His unfinished task, and that he later met and conversed with Moses and Buddha" (pp. 129–130).

Dr. Deutsch accuses me of an "anti-Unification Church polemic," saying that *Cults* was not designed to attack or defend any group. However, Dr. Galanter's polemic against other cults spares Moon to be praised by faint damnation.

Dr. Galanter's previous publications bear relevance, but not because they testify to the merits of this book. His earlier articles chronicled research involving the Unification Church but none involving Synanon or the People's Temple, two groups the author found particularly objectionable.

Dr. Deutsch describes the book's essence as explaining "how highly ideological, cohesive groups... exert their powerful influence over their members' beliefs and behavior." However, common sense suggests a hypothesis that such intense group forces could influence intelligent and sincere researchers who spend countless hours studying the source of these forces.

Dr. Roth asserts that I believe *Cults* was doomed to be biased; I simply found it to be biased and then wondered why. He says that "unconscious bias is a hard charge for any of us to dispel completely" and asks if any of us is objective. But unconscious bias is not a cardinal sin; it becomes troublesome only when we fail to know ourselves and use denial when confronted with our biases.

Dr. Deutsch was present when research proposals were made to Unification Church leaders, and he states that no deals were made. Although he thus dismisses conscious bias, he overlooks the possibility of unconscious bias, since he himself was a participant in research that led to the book.

Mr. Gutman concedes that his law firm has represented the Unification Church, along with similar groups, but corrects my assertion that the church had been his largest client. He further asserts that the identity and size of his client groups are irrelevant. I would commend Dr. Roth's letter to Mr. Gutman's attention; unconscious bias can affect anyone.

I cannot agree with Dr. Roth that cults have been a taboo for psychiatrists. I find many psychiatrists simply uninterested in cults, and a paucity of grants for research on cults does not help. If there is any taboo among us, it is discussing Scientology, which for several decades has been bullying its critics and discrediting our profession and which the book did not mention at all.

JOHN HOCHMAN, M.D.
Tarzana, Calif.

Hemlock Society Newsletter

SIR: A patient recently gave me a copy of the *Hemlock Quarterly*, which is a newsletter of the Hemlock Society. As a psychiatrist I was disturbed by this publication, which gave specific drug dosages and stated the usual lethal dose, as well as other specific recommendations for ensuring one's death by suicide. Also included were specific recommendations for asphyxiation.

My patient was equally upset by the newsletter. Although she is now feeling better, she has in the past experienced periods of serious suicidal impulses and felt that if such information had been available to her at those times, she might have been more readily and easily moved to attempt suicide. It is important for psychiatrists to be aware of the open dissemination of such specific information about potentially lethal substances, which can only increase the possibility of successful self-destruction by depressed patients during periods of suicidal despair.

THOMAS H. VAN DOREN, M.D.
Kalamazoo, Mich.

Reprints of letters to the Editor are not available.

Homosexuality and the Armed Services

This position statement was proposed by the Committee on Gay, Lesbian, and Bisexual Issues[1] of the Council on National Affairs. It was approved by the Assembly of District Branches in November 1990 and by the Board of Trustees in December 1990.

APA, since 1973, has formally opposed all public and private discrimination against homosexuals in such areas as employment, housing, public accommodations, and licensing. It follows that APA opposes exclusion and dismissal from the armed services on the basis of sexual orientation. Furthermore, APA asserts that no burden of proof of judgment, capacity, or reliability should be placed on homosexuals which is greater than that imposed on any other persons within the armed services.

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[1] The committee members are Robert Paul Cabaj, M.D. (chairperson and Assembly liaison), Richard A. Isay, M.D., Margery Sved, M.D., Rochelle Lynn Klinger, M.D., Marshall Forstein, M.D., and Peggy Hanley-Hackenbruck, M.D. (corresponding member).

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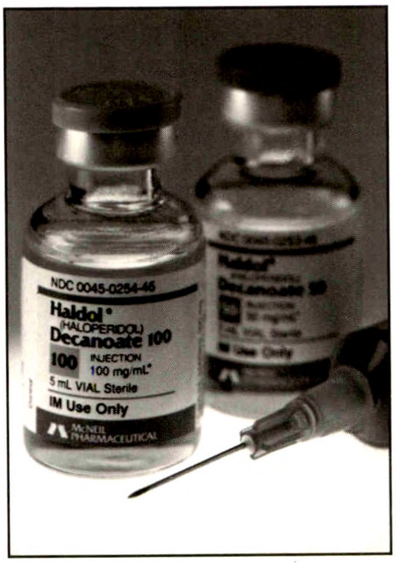
Contraindications: Since the pharmacologic and clinical actions of HALDOL Decanoate 50 and HALDOL Decanoate 100 are attributed to HALDOL haloperidol as the active medication, Contraindications, Warnings, and additional information are those of HALDOL, modified to reflect the prolonged action.

HALDOL is contraindicated in severe toxic central nervous system depression or comatose states from any cause and in individuals who are hypersensitive to this drug or have Parkinson's disease.

Warnings: *Tardive Dyskinesia:* Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown. Both the risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown. Given these considerations, antipsychotic drugs should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that 1) is known to respond to antipsychotic drugs, and 2) for whom alternative, equally effective, but potentially less harmful treatments are **not** available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically. If signs and symptoms of tardive dyskinesia appear in a patient on antipsychotics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome. (For further information about the description of tardive dyskinesia and its clinical detection, please refer to ADVERSE REACTIONS.)



Neuroleptic Malignant Syndrome (NMS): A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status (including catatonic signs) and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis) and acute renal failure. The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system (CNS) pathology. The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS. If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported. Hyperpyrexia and heat stroke, not associated with the above symptom complex, have also been reported with HALDOL.

Usage in Pregnancy: (see PRECAUTIONS—Usage in Pregnancy) *Combined Use With Lithium:* (see PRECAUTIONS—Drug Interactions)

General: Bronchopneumonia, sometimes fatal, has followed use of antipsychotic drugs, incuding haloperidol. Prompt remedial therapy should be instituted if dehydration, hemoconcentration or reduced pulmonary ventilation occur, especially in the elderly. Decreased serum cholesterol and/or cutaneous and ocular changes have been reported with chemically-related drugs, although not with haloperidol. See PRECAUTIONS—Information for Patients for information on mental and/or physical abilities and on concomitant use with other substances.

Precautions: Administer cautiously to patients: (1) with severe cardiovascular disorders, due to the possibility of transient hypotension and/or precipitation of anginal pain (if a vasopressor is required, epinephrine should not be used since HALDOL may block its vasopressor activity and paradoxical further lowering of blood pressure may occur; metaraminol, phenylephrine or norepinephrine should be used; (2) receiving anticonvulsant medications, with a history of seizures, or with EEG abnormalities, because HALDOL may lower the convulsive threshold. If indicated, adequate anticonvulsant therapy should be concomitantly maintained; (3) with known allergies or a history of allergic reactions to drugs; (4) receiving anticoagulants, since an isolated instance of interference occurred with the effects of one anticoagulant (phenindione). Concomitant antiparkinson medication, if required, may have to be continued after HALDOL is discontinued because of different excretion rates; if both are discontinued simultaneously, extrapyramidal symptoms may occur. Intraocular pressure may increase when anticholinergic drugs, including antiparkinson drugs, are administered concomitantly with HALDOL. When HALDOL is used for mania in bipolar disorders, there may be a rapid mood swing to depression. Severe neurotoxicity may occur in patients with thyrotoxicosis receiving antipsychotic medication, including HALDOL.

The 1, 5, 10 mg HALDOL tablets contain FD&C Yellow No. 5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible individuals, especially in those who have aspirin hypersensitivity.

Information for Patients: Mental and/or physical abilities required for hazardous tasks or driving may be impaired. Alcohol should be avoided due to possible additive effects and hypotension.

Drug Interactions: Patients receiving lithium plus haloperidol should be monitored closely for early evidence of neurological toxicity and treatment discontinued promptly if such signs appear. As with other antipsychotic agents, it should be noted that HALDOL may be capable of potentiating CNS depressants such as anesthetics, opiates, and alcohol.

Carcinogenesis, Mutagenesis and Impairment of Fertility: No mutagenic potential of haloperidol decanoate was found in the Ames Salmonella microsomal activation assay.

Carcinogenicity studies using oral haloperidol were conducted in Wistar rats (dosed at up to 5 mg/kg daily for 24 months) and in Albino Swiss mice (dosed at up to 5 mg/kg daily for 18 months). In the rat study survival was less than optimal in all dose groups, reducing the number of rats at risk for developing tumors. However, although a relatively greater number of rats survived to the end of the study in high dose male and female groups, these animals did not have a greater incidence of tumors than control animals. Therefore, although not optimal, this study does suggest the absence of a haloperidol related increase in the incidence of neoplasia in rats at doses up to 20 times the usual daily human dose for chronic or resistant patients. In female mice at 5 and 20 times the highest initial daily dose for chronic or resistant patients, there was a statistically significant increase in mammary gland neoplasia and total tumor incidence; at 20 times the same daily dose there was a statistically significant increase in pituitary gland neoplasia. In male mice, no statistically significant differences in incidences of total tumors or specific tumor types were noted.

Antipsychotic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent *in vitro*, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of antipsychotic drugs. Neither clinical studies nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is considered too limited to be conclusive at this time.

Usage in Pregnancy: Pregnancy Category C. Safe use in pregnancy or in women likely to become pregnant has not been established; use only if benefit clearly justifies potential hazards to the fetus.

Nursing Mothers: Infants should not be nursed during drug treatment.

Pediatric Use: Controlled trials to establish the safety and effectiveness of intramuscular administration in children have not been conducted.

Adverse Reactions: Adverse reactions following the administration of HALDOL Decanoate 50 or HALDOL Decanoate 100 are those of HALDOL haloperidol. Since vast experience has accumulated with HALDOL, the adverse reactions are reported for that compound as well as for haloperidol decanoate. As with all injectable medications, local tissue reactions have been reported with haloperidol decanoate.

CNS Effects: Extrapyramidal Reactions—Neuromuscular (extrapyramidal) reactions have been reported frequently, often during the first few days of treatment. Generally they involved Parkinson-like symptoms which when first observed were usually mild to moderately severe and usually reversible. Other types of neuromuscular reactions (motor restlessness, dystonia, akathisia, hyperreflexia, opisthotonos, oculogyric crises) have been reported far less frequently, but were often more severe. Severe extrapyramidal reactions have been reported at relatively low doses. Generally, extrapyramidal symptoms are dose-related since they occur at relatively high doses and disappear or become less severe when the dose is reduced. Antiparkinson drugs may be required. Persistent extrapyramidal reactions have been reported and the drug may have to be discontinued in such cases. *Withdrawal Emergent Neurological Signs*—Abrupt discontinuation of short-term antipsychotic therapy is generally uneventful. However, some patients on maintenance treatment experience transient dyskinetic signs after abrupt withdrawal. In certain cases these are indistinguishable from "Tardive Dyskinesia" except for duration. It is unknown whether gradual withdrawal will reduce the occurrence of these signs, but until further evidence is available HALDOL should be gradually withdrawn. *Tardive Dyskinesia*—As with all antipsychotic agents HALDOL has been associated with persistent dyskinesias. Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may appear in some patients on long-term therapy or may occur after drug therapy has been discontinued. The risk appears to be greater in elderly patients on high-dose therapy, especially females. The symptoms are persistent and in some patients irreversible. The syndrome is characterized by rhythmical involuntary movements of tongue, face, mouth or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movements of extremities and the trunk. There is no known effective treatment for tardive dyskinesia; antiparkinson agents usually do not alleviate the symptoms of this syndrome. It is suggested that all antipsychotic agents be discontinued if these symptoms appear. Should it be necessary to reinstitute treatment, or increase the dosage of the agent, or switch to a different antipsychotic agent, this syndrome may be masked. It has been reported that fine vermicular movement of the tongue may be an early sign of tardive dyskinesia and if the medication is stopped at that time the full syndrome may not develop. *Tardive Dystonia*—Tardive dystonia, not associated with the above syndrome, has also been reported. Tardive dystonia is characterized by delayed onset of choreic or dystonic movements, is often persistent, and has the potential of becoming irreversible. *Other CNS Effects*—Insomnia, restlessness, anxiety, euphoria, agitation, drowsiness, depression, lethargy, headache, confusion, vertigo, grand mal seizures, and exacerbation of psychotic symptoms including hallucinations, and catatonic-like behavioral states which may be responsive to drug withdrawal and/or treatment with anticholinergic drugs.

Body as a Whole: Neuroleptic malignant syndrome (NMS), hyperpyrexia and heat stroke have been reported with HALDOL. (See WARNINGS for further information concerning NMS.) *Cardiovascular Effects:* Tachycardia, hypotension, hypertension and ECG changes. *Hematologic Effects:* Reports of mild, usually transient leukopenia and leukocytosis, minimal decreases in red blood cell counts, anemia, or a tendency toward lymphomonocytosis; agranulocytosis rarely reported and only in association with other medication. *Liver Effects:* Impaired liver function and/or jaundice. *Dermatologic Reactions:* Maculopapular and acneiform reactions, isolated cases of photosensitivity, loss of hair. *Endocrine Disorders:* Lactation, breast engorgment, mastalgia, menstrual irregularities, gynecomastia, impotence, increased libido, hyperglycemia, hypoglycemia and hyponatremia. *Gastrointestinal Effects:* Anorexia, constipation, diarrhea, hypersalivation, dyspepsia, nausea and vomiting. *Autonomic Reactions:* Dry mouth, blurred vision, urinary retention, diaphoresis, and priapism. *Respiratory Effects:* Laryngospasm, bronchospasm and increased depth of respiration. *Special Senses:* Cataracts, retinopathy and visual disturbances. *Other:* Cases of sudden and unexpected death have been reported in association with the administration of HALDOL. The nature of the evidence makes it impossible to determine definitively what role, if any, HALDOL played in the outcome of the reported cases. The possibility that HALDOL caused death cannot, of course, be excluded, but it is to be kept in mind that sudden and unexpected death may occur in psychotic patients when they go untreated or when they are treated with other antipsychotic drugs.

IMPORTANT: Full directions for use should be read before HALDOL or HALDOL Decanoate products are administered or prescribed.

For information on symptoms and treatment of overdosage, see full prescribing information.

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- ▲ Convenient, once-a-month dosing
- ▲ Less need for anticholinergics—a proven decrease in the number of patients requiring anticholinergics, over time[1]

During dose adjustment or episodes of exacerbation of psychotic symptoms, therapy with HALDOL Decanoate 100 or HALDOL Decanoate 50 can be supplemented with short-acting forms of HALDOL® (haloperidol). The side effects of the decanoate products are those of HALDOL. The prolonged action of HALDOL Decanoate 100 and HALDOL Decanoate 50 should be considered in the management of side effects.

Please see brief summary of Prescribing Information on adjacent page.

Start depot therapy with **HALDOL® Decanoate 100**

(HALOPERIDOL) INJECTION 100mg/mL

Reference

1. Youssef HA. A five-year follow-up study of chronic schizophrenics and other psychotics treated in the community: depot haloperidol decanoate versus other neuroleptics. *Advances in Therapy.* 1989;6(4):186-195.

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